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Abstract: OBJECTIVES Clinical trial registration is widely recommended because it allows tracking of trials that helps ensure full and unbiased reporting of their results. The aim of the present overview was to provide empirical evidence on bias associated with trial registration via a meta-epidemiological approach. STUDY DESIGN AND SETTINGS Six databases were searched in September 2017 for randomized clinical trials and systematic reviews thereof assessing the effects of orthodontic clinical interventions. After duplicate study selection and data extraction, statistical analysis included a two-step meta-epidemiological approach within- and across-included meta-analyses with a Paule-Mandel random-effects model to calculate differences in standardized mean differences (ΔSMD) between registered and unregistered trials and their 95% confidence intervals (CI), followed by subgroup and sensitivity analyses. RESULTS A total of 16 meta-analyses with 83 trials and 4,988 patients collectively were finally included, which indicated that registered trials reported less beneficial treatment effects than unregistered trials (ΔSMD = -0.36; 95% CI = -0.60, -0.12). Although some small-study effects were identified, sensitivity analyses according to precision and risk of bias indicated robustness. CONCLUSION Signs of bias from lack of trial protocol registration were found with nonregistered trials reporting more beneficial intervention effects than registered ones. Caution is warranted by the interpretation of nonregistered randomized trials or systematic reviews thereof.

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Registered trials report less beneficial treatment effects than unregistered ones: a meta-epidemiological study in orthodontics

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Abstract

Objectives: Clinical trial registration is widely recommended, since it allows tracking of trials that helps ensure full and unbiased reporting of their results. Aim of the present overview was to provide empirical evidence on bias associated with trial registration via a meta-epidemiological approach.

Study Design and Settings: Six databases were searched in September 2017 for randomized clinical trials and systematic reviews thereof assessing the effects of orthodontic clinical interventions. After duplicate study selection and data extraction, statistical analysis included a two-step meta-epidemiological approach within- and across-included meta-analyses with a Paule-Mandel random-effects model to calculate Differences in Standardized Mean Differences (ΔSMD) between registered and unregistered trials and their 95% Confidence Intervals (CI), followed by subgroup and sensitivity analyses.

Results: A total of 16 meta-analyses with 83 trials and 4988 patients collectively were finally included, which indicated that registered trials reported less beneficial treatment effects than unregistered trials (ΔSMD=-0.36; 95% CI=-0.60,-0.12). Although some small-study effects were identified, sensitivity analyses according to precision and risk of bias indicated robustness.

Conclusions: Signs of bias from lack of trial protocol registration were found with non-registered trials reporting more beneficial intervention effects than registered ones. Caution is warranted by the interpretation of non-registered randomized trials or systematic reviews thereof.

Keywords: Randomized clinical trials; Protocol registration; Empirical bias; Meta-analysis; Meta-epidemiology

Manuscript

1. Introduction

1.1. Background

Randomized clinical trials are regarded as the gold standard in comparative efficacy research and form the basis for translating research evidence to clinical practice [1]. Among their advantages, methodological transparency is crucial and entails registration of the trial design protocol in a public domain prior to trial initiation in order to improve accountability in the conduct and reporting of research [2]. Trial protocols can be used post hoc to compare the original plan with subsequent procedures and analyses [3], thereby potentially reducing the risk of data dredging. *A priori* trial registration can additionally safeguard against bias-related phenomena such as delayed publication or non-publication of trials, selective reporting of outcomes, manipulation of the analysis plan, and counting covert duplicate publications within systematic reviews as separate trials [3-6].

Insights on trial characteristics systematically associated with treatment effects can be gleamed through meta-epidemiological studies. This is a subgenre of the big family of overviews of reviews, wherein data from a collection of meta-analyses is integrated and classified according to a specific study-level trait in order to empirically assess its influence on treatment effects [7].

A recent comprehensive meta-epidemiological study reported that non-registered or retrospectively registered trials tend to show larger treatment effects [8]. Although the effect was not statistically significant, this is confirmed by cross-sectional overviews of randomized trials in cardiology [9] or general medicine [10] that report weak associations between positive findings and trial registration, although the effects were not always consistent. It is also important to note that these analyses were based on qualitative evaluations of trial results by using either a P value cut-off or the trialists' interpretation of the results in text, both of which can be problematic.

1.2. Scope

The aim of this meta-epidemiological study is to provide empirical evidence of possible differences in the results of registered and non-registered randomized clinical trials in orthodontics as a sign of bias, including its direction and magnitude.

2. Methods

2.1. Protocol, eligibility criteria, and registration

The protocol for this overview of reviews and trials was made *a priori* based loosely on the format of a systematic review, registered in PROSPERO (CRD42017072043), and all *post hoc* changes to the protocol were appropriately noted. According to the criteria set a priori, eligibility included parallel randomized clinical trials (or meta-analyses thereof) on human patients on any experimental intervention compared to a conventional or control group with any binary/continuous outcome in orthodontics and dentofacial orthopedics. Excluded were non-clinical studies, animal studies, and non-randomized studies. Split-mouth (within-person) randomized clinical trials were excluded as the suboptimal reporting of such studies in orthodontics makes their integration in meta-epidemiological synthesis difficult [11, 12]. Additionally, only 'hard' outcomes pertaining to overall treatment success, treatment duration, or treatment adverse effects were included, because these can easily be categorized as beneficial/detrimental and are empirically more robust than surrogate outcomes [13]. Ultimately, only meta-analyses of at least three trials, including at least one registered and at least one non-registered trial were included so that meta-epidemiological effects can be estimated. This meta-epidemiological study is loosely conducted and reported according to guidelines for systematic reviews and overviews thereof [1, 7, 14].

2.2. Information sources and literature search

The literature search for this study was done in two steps. Initially data from a recent study [15] that searched the ClinicalTrials.gov and the ISRCTN registries were used to identify all orthodontic subjects with at least one registered randomized trial (Supplementary Table 1). Then, separate literature searches were performed for all identified subjects in order to identify eligible registered or non-registered randomized trials or systematic reviews with meta-analyses, including at least one randomized trial. A total of six electronic databases (MEDLINE through Pubmed, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Database of Abstracts of Reviews of Effects, Web of Knowledge, and Scopus) were searched systematically by one author (SNP) without any limitations from inception up to September 2nd, 2017 (Supplementary Table 2). Four additional sources (Scopus, Google Scholar, ClinicalTrials.gov, and ISRCTN registry) were manually searched for additional trials. No limitations concerning language, publication year or status were applied. All identified relevant systematic reviews with meta-analysis were manually searched for additional trials.

2.3. Study selection, data collection, and risk of bias in individual studies

The titles and abstracts of all studies identified by the literature searches were screened by one author (SNP), excluding all those obviously non-relevant according to the study scope and non-clinical studies. The remaining full texts were checked for eligibility by one author (SNP) with a subsequent duplicate independent checking in full by another author (GMX), while conflicts were resolved by the last two authors (MTC, TE). All identified randomized trials were separately checked for eligibility on study design, intervention, and outcome. All meta-analyses included in identified systematic reviews were checked for any eligible randomized trials that could be added to a single meta-analysis without overlap on each topic and outcome to inform the meta-epidemiological synthesis. Trial overlaps within each meta-analysis and across meta-analyses were removed by assigning the Pubmed unique identifier to each trial and including each trial only once per meta-analysis. Where needed, interquartile ranges were converted to standard deviations and similar measurements concerning the same outcome (like visual analogue and Likert pain scales) were combined. When subgroup analyses were performed in identified meta-analyses, these were ignored and the overall pooled estimate was used.

Characteristics of included meta-analysis and trials were extracted fully in duplicate by two authors (SNP, GMX) using pre-determined and piloted extraction forms. Extracted data included first author name, publication year, outcome measured, outcome data, and trial registration status. Registration status originated from a previous study on two trial registers [15] and was subsequently supplemented by reading the full text of the published paper. Missing data were requested by trialists or calculated from available high-quality graphs with the freely-available Web Plot Digitizer version 3.12 (http://arohatgi.info/WebPlotDigitizer).

The risk of bias of the included randomized trials was not planned to be comprehensively assessed with the Cochrane risk of bias tool [1], as this was outside the scope of this study. Only the adequacy of the generation of random sequence and blinding of outcome assessor was assessed independently by two authors (SNP, GMX) according to the Cochrane guidelines [1] as low or unclear/high to use this for sensitivity analyses. Differences in risk of bias between registered and non-registered trials were gauged with cross-tabulation and calculation of relative risks and their 95% Confidence Intervals (CI).

2.4. Data synthesis

As the clinical effects of orthodontic trials are bound to be influenced by appliance [16, 17], patient [18], or study design-related characteristics [6, 19, 20] a random-effects model was chosen a priori, even though no clear guidance for model choice in meta-epidemiological studies exists. The Paule-Mandel random-effects variance estimator was preferred to the DerSimonian and Laird one, following recent advice [21].

For all included meta-analyses, the Standardized Mean Difference (SMD) was chosen as the effect measure because it standardizes estimates by their variability and enables overall synthesis [22]. Binary outcomes were planned to be converted to SMDs prior to pooling, but no eligible binary outcomes were identified. All outcomes were categorized as beneficial or harmful and all SMDs were recoded on the same direction, so that a positive SMD was beneficial. When trials with more than one experimental (interventional) trial arms were included, these arms were pooled prior to the meta-analysis to avoid double-counting of control patients.

Random-effects meta-regression with the Paule-Mandel variance estimator was performed, fully incorporating heterogeneity between-trials, to derive a difference in SMDs (ΔSMD) and the standard error within each meta-analysis, according to registration status of included trials. Ultimately, Paule-Mandel random-effects meta-analysis (i.e. meta-epidemiological synthesis) was used to pool the overall effect of trial registration across all component meta-analyses taking into account variability across them. The magnitude for SMDs and ΔSMD was arbitrarily assessed using Cohen's [22] guidelines: up to 0.2=small effect, 0.2 to 0.5=medium effect, 0.5 to 0.8=large effect, and larger than 0.8=very large effect. These cut-off values were also adopted to visually enhance the produced forest plot [23].

Absolute and relative between-meta-analyses heterogeneity/inconsistency was quantified with the tau^2 metric and the I^2 statistic, respectively. The latter is defined as the proportion of total variability in the results explained by heterogeneity, and not chance [24]. 95% CIs around all heterogeneity measures were calculated to quantify existing uncertainty [25], while 95% predictive intervals were to be calculated for the meta-epidemiological synthesis to provide a range of possible effects for a future clinical setting

[26]. All analyses were run in Stata SE 14.0 (StataCorp, College Station, TX) by one author (SNP) and all material was openly made available through Zenodo [27]. A two-tailed P-value of 0.05 was considered significant for hypothesis-testing, except for a 0.10 used for the test of heterogeneity and reporting biases, due to low power [28].

2.5. Additional analyses

Random-effects subgroup analyses were planned a priori to identify possible differences in the effect of trial registration among various orthodontic topics, binary versus continuous outcomes, subjective versus objective outcomes, and positive or negative effect direction with an interaction term by Paule-Mandel meta-regression. Indications of reporting biases (including small-study effects) were assessed with Egger's linear regression test [29] and contour-enhanced funnel plots [30].

Robustness of the results to possible sources of bias or confounding was planned to be checked in sensitivity analyses by (i) including only meta-analyses with an arbitrary cut-off of at least 10 trials/meta-analysis, (ii) comparing the results of fixed-effect and random-effects models, and (iii) including only the largest meta-analysis from each included Intervention-Control comparison. Additionally, (iv) a post hoc sensitivity analysis by including the 50% of meta-analyses with most included trialswas performed after identifying signs of small-study effects. Finally, (v) a sensitivity analysis was performed to account for different risk of bias for the randomization sequence generation or (vi) for the blinding of outcome measurement across trials by including both trial registration and bias as factors in the within-meta-analysis meta-regression of meta-analyses with at least 5 trials, before pooling the overall effect of trial registration across meta-analyses.

3. Results

3.1. Study selection

The literature search yielded a total of 1241 hits electronically and 18 hits manually as of September 2, 2017; 216 of which, proceeded to full text assessment after eliminating duplicates and ineligible studies by title or abstract (Figure 1; Supplementary Table 3a-3g). Finally, a total of 48 trials on similar comparisons were identified as eligible for inclusion in the present meta-epidemiological study. These were included in 16 separate meta-analyses on seven different topics, with some trial overlap among meta-analyses. Four authors of identified studies were also contacted to request missing data (Supplementary Table 4), which were provided.

3.2. Study characteristics

The 16 eligible meta-analyses included a total of 83 trials with overlap (median of 3.5 trials; interquartile range 3 to 6 trials; range 3 to 14 trials) and a total of 4988 randomized patients (median of 47 patients; interquartile range 30 to 60 patients; range 14 to 1000 patients). Analyzing the characteristics of included trials without overlap, a total of 59 published reports pertaining to 48 unique randomized trials were identified (Supplementary Table 5), which randomized a median of 40 patients (interquartile range 30 to 60 patients; range 14 to 1000 patients) to a total of 3188 patients. Among these 48 trials, only 10 of them (20.8%) had been registered in a trial registry overall, with registered trials within each meta-analysis ranging from 10% to 66% (Supplemenary Table 6). A wide variety of outcomes were assessed in these trials including treatment duration, dental or skeletal treatment, and adverse effects like patient-reported pain or treatment-induced root resorption.

3.3. Risk of bias within studies

Hints of bias (i.e. systematic differences in the results) within included trials was primarily addressed according to their registration status. Additionally, the adequacy of the random sequence generation was formally assessed according to the Cochrane risk of bias tool. From the 48 identified trials, low risk of bias was found for the randomization sequence in 32 trials (66.7%), while the rest of the trials had either unclear or high risk of bias. Adequate blinding of outcome assessment was found for 15 of the 48 (31.3%) identified trials. Registered trials were more likely to have low risk of bias for the randomization generation (90.0% vs 60.5%, respectively; relative risk: 1.49; 95% CI: 1.07 to 2.07) and more likely to have low risk of bias for blinding of outcome assessors (93.3% vs 54.6%; relative risk: 1.38; 95% CI: 0.56 to 3.43).

3.4. Results of individual meta-analyses and meta-epidemiological synthesis

The results of all included meta-analyses including the registration status and risk of bias for randomization or blinding of outcome assessor can be seen in full detail in Supplementary Figure.

The meta-epidemiological synthesis of all 16 included meta-analyses indicated that considerable differences in the reported intervention effects were seen between registered and non-registered trials (pooled ΔSMD: -0.36; 95% CI: -0.60, -0.12; P: 0.003). This indicated that registered trials reported less favorable intervention effects compared to non-registered trials, which could be interpreted as signs of bias. Based on Cohen's classification, this bias would be judged as of moderate magnitude. The observed absolute (tau^2: 0; 95% CI: 0, 0.18) and relative heterogeneity (I^2: 0%; 95% CI: 0%, 42%) was minimal and the 95% predictive intervals coincided with the 95% CIs.

3.5. Additional analyses

No robust evidence could be found for differences among subgroups according to clinical scenario, outcome scope, nature, or direction (Table 1). Although great variation was seen (especially for the different clinical scenarios), very wide 95% CI were observed, indicating imprecision due to break-up of the sample.

As far as reporting biases are concerned, the funnel plot gave clear signs of asymmetry, which were formally confirmed by Egger's test (coefficient=-0.88; 95% CI=-1.59, -0.18; P=0.02). Based on the funnel plot the source of this asymmetry was taken to be small-study effects, with smaller and more imprecise meta-analyses reporting greater ΔSMDs.

A number of pre-defined sensitivity analyses were performed on the main analysis (Table 2). Choice of statistical model or choice of only one meta-analysis per clinical scenario was not associated with the observed effects. Due to significant signs of small-study effects an additional *post hoc* sensitivity analysis with only the 50% largest meta-analyses was performed, which yielded identical ΔSMD. Additionally, a separate sensitivity analysis controlling for low or unclear/high risk of bias for the generation of the randomization sequence found likewise that the observed effects were robust (ΔSMDs of -0.36 and -0.37 for the original and adjusted analysis, respectively). Finally, a separate sensitivity analysis controlling for low or unclear/high risk of bias for blinding outcome assessment found that trial registration had considerably higher influence on the observed effects (ΔSMDs of -0.36 and -1.80 for the original and adjusted analysis, respectively), but caution is needed as only 3 meta-analyses contributed to this.

4. Discussion

4.1. Principal findings

The present review summarizes empirical evidence up to September 2017 about the effects of trial registration on the results of orthodontic randomized clinical trials. Empirical evidence from 16 meta-analyses and 4-988 patients indicated that registered trials report considerably less beneficial treatment effects compared to non-registered trials, which can be interpreted as signs of bias of moderate magnitude. The fact that bias from lack of registration was found to be of moderate magnitude must not be underestimated, since this source of bias can act in an additive manner together with other known bias-related sources, such as~~,~~ inadequate randomization or baseline imbalance, lack of blinding, small sample size, choice of control group, and others [19, 31-36].

4.2. Comparison with other studies

To our knowledge this is the first study to provide statistically significant empirical evidence of bias from lack of trial registration in an oral health field. The only study similar to ours is the comprehensive meta-epidemiological study from Dechartres et al. [8], who assessed Cochrane Reviews with binary outcomes published between 2011 and 2014. Although they included a greater number of meta-analyses (n=37) across various medical fields, they found a small effect indicating that non-registered trials tended to show larger treatment effect estimates than registered trials (ratio of odds ratios=0.85; 95% CI=0.67-1.08), which was not statistically significant. Differences with our results could be explained by the inclusion in the Dechartres et al. [8] study of more heterogeneous trial outcomes than the present study, where only 'hard' outcomes were included. Additionally, Dechartres et al. [8] found similar magnitude of bias for non-registered versus registered trials (ratio of odds ratios of 0.85)—although not statistically significant. Another cross-sectional overview of randomized trials found only a weak association between trial registration and positive study results (adjusted risk ratio of 0.87) and a possible variation between non-industry and industry funded trials [10], but concluded that evidence is inconsistent. However, it must be noted that this was a large unselected group of randomized trials across various research question and unstratified by disease, intervention, and outcome and therefore, a potentially existing effect might have been masked by the pooled analysis.

4.3. Strengths and limitations

Strengths of the current study include the *a priori* development of a research protocol that was precisely followed and the detailed reporting of all post hoc choices (Appendix), which supports the study's credibility [37]. Additionally, maximized data output through author communications, use of an improved variance estimator [21], graphical assessment of the effects' clinical relevance with contours of magnitude [38], and transparent open data provision [27] can be counted among the study's strengths.

This study also has some limitations. First, it was based on a convenience sample limited to a dental specialty field, which meant that only a small number of eligible trials could eventually be included and that the meta-epidemiological synthesis might be potentially underpowered. Therefore, additional empirical evidence is needed to confirm or refute the findings of the current study. Second, as only studies from a single field were included, the studies results might not directly transferable to other field, although no rationale for this exists. Third, trial registration might be associated with many other trial characteristics possibly linked to bias like geographic origin, number of study centers, sample size and used methods, which was not considered in this study. Finally, we did not differentiate between randomized trials having been prospectively or retrospectively registered and we did not directly assess firsthand discrepancies between the trials' published reports and protocols. These were not planned during protocol and it would not be possible to formally integrate those factors in the analysis, due to the already limited existing material. This can be the focus of future empirical studies with a wider scope.

4.4. Conclusions and policy implications

It is evident from the results of this study that trial registration, apart from being crucial to the transparency and credibility of a trial, can potentially influence either directly or indirectly the current evidence base and therefore clinical recommendations. Our findings support the the initiatives of the World Health Organization, the International Committee of Medical Journal Editors towards, and other research regulatory authorities to provide a depository for trial registration and to promote policies that support trial registration and adherence to reporting guidelines. The current situation of clinical trials in orthodontics suboptimal both in terms of registration [15] and reporting quality [39]. Efforts have been made from orthodontic journals to improve author adherence to the Consolidated Standards of Reporting Trials (CONSORT) guidelines [40]. However and even though a large part of medical journals requires all submitted trials to be registered [41], only five out of the ten existing orthodontic journals only mention trial registration in their author instructions, while only one (Journal of Orthodontics) words this explicitly as a requirement for publication [15]. It is important finally to note that trial registration does not preclude the use of inappropriate methods or bias.

4.5. Summary

The present meta-epidemiological study provides empirical evidence of bias originating from a lack of protocol registration among randomized clinical trials in orthodontics and dentofacial orthopaedics. Therefore, caution is warranted by the interpretation of unregistered trials or by their incorporation in systematic reviews and clinical guidelines. However, the evidence base that was used in the present study is limited and future studies are expected to expand upon it.

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Data availability

The datasets and commands of this study are openly available through Zenodo (http://doi.org/10.5281/zenodo.1186318).

References

[1] Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available at: www.cochrane-handbook.org. Accessed September 26th 2017.

[2] De Angelis C, Drazen JM, Frizelle FA, et al. International Committee of Medical Journal Editors. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. Lancet 2004;356:911–2.

[3] Dwan K, Altman DG, Cresswell L, Blundell M, Gamble CL, Williamson PR. Comparison of protocols and registry entries to published reports for randomised controlled trials. Cochrane Database Syst Rev 2011;1:MR000031.

[4] Tramèr MR, Reynolds DJ, Moore RA, McQuay HJ. Impact of covert duplicate publication on meta-analysis: a case study. BMJ 1997;315:635–40.

[5] Song F, Eastwood AJ, Gilbody S, Duley L, Sutton AJ. Publication and related biases. Health Technol Assess 2000;4:1–115.

[6] Papageorgiou SN, Kloukos D, Petridis H, Pandis N. Publication of statistically significant research findings in prosthodontics & implant dentistry in the context of other dental specialties. J Dent 2015;43:1195–202.

[7] Dechartres A, Trinquart L, Faber T, Ravaud P. Empirical evaluation of which trial characteristics are associated with treatment effect estimates. J Clin Epidemiol 2016;77:24-37.

[8] Dechartres A, Ravaud P, Atal I, Riveros C, Boutron I. Association between trial registration and treatment effect estimates: a meta-epidemiological study. BMC Med 2016;14:100.

[9] Emdin C, Odutayo A, Hsiao A, et al. Association of cardiovascular trial registration with positive study findings: Epidemiological Study of Randomized Trials (ESORT). JAMA Intern Med 2014;356.

[10] Odutayo A, Emdin CA, Hsiao AJ, et al. Association between trial registration and positive study findings: cross sectional study (Epidemiological Study of Randomized Trials-ESORT). BMJ 2017;356:j917.

[11] Lesaffre E, Garcia Zattera MJ, Redmond C, Huber H, Needleman I; ISCB Subcommittee on Dentistry. Reported methodological quality of split-mouth studies. J Clin Periodontol 2007;34:756–61.

[12] Koletsi D, Pandis N, Polychronopoulou A, Eliades T. Does published orthodontic research account for clustering effects during statistical data analysis? Eur J Orthod 2012;34:287–92.

[13] Ciani O, Buyse M, Garside R, et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomised controlled trials: meta-epidemiological study. BMJ 2013;346:f457.

[14] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 2009;62:e1–e34.

[15] Papageorgiou SN, Antonoglou GN, Sándor GK, Eliades T. Randomized clinical trials in orthodontics are rarely registered a priori and often published late or not at all. PLoS One 2017;12:e0182785.

[16] Papageorgiou SN, Konstantinidis I, Papadopoulou K, Jäger A, Bourauel C. Clinical effects of pre-adjusted edgewise orthodontic brackets: a systematic review and meta-analysis. Eur J Orthod 2014;36:350–63.

[17] Papageorgiou SN, Gölz L, Jäger A, Eliades T, Bourauel C. Lingual vs. labial fixed orthodontic appliances: systematic review and meta-analysis of treatment effects. Eur J Oral Sci 2016;124:105–18.

[18] Saloom HF, Papageorgiou SN, Carpenter GH, Cobourne MT. Impact of obesity on orthodontic tooth movement in adolescents: a prospective clinical cohort study. J Dent Res 2017;96:547–54.

[19] Papageorgiou SN, Antonoglou GN, Tsiranidou E, Jepsen S, Jäger A. Bias and small-study effects influence treatment effect estimates: a meta-epidemiological study in oral medicine. J Clin Epidemiol 2014;67:984–92.

[20] Papageorgiou SN, Xavier GM, Cobourne MT. Basic study design influences the results of orthodontic clinical investigations. J Clin Epidemiol 2015;68:1512–22.

[21] Veroniki AA, Jackson D, Viechtbauer W, et al. Methods to estimate the between-study variance and its uncertainty in meta-analysis. Res Synth Methods 2016;7:55–79.

[22] Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. New York: Academic Press; 1988.

[23] Papageorgiou SN. Meta-analysis for orthodontists: Part II--Is all that glitters gold? J Orthod 2014;41:327–36.

[24] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.

[25] Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc 2009;172:137–59.

[26] IntHout J, Ioannidis JP, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open 2016;6:e010247.

[27] Papageorgiou SN, Xavier GM, Cobourne MT, Eliades T. Registered trials report less beneficial treatment effects than unregistered ones: a meta-epidemiological study in orthodontics [Data set]. Zenodo. http://doi.org/10.5281/zenodo.1186318.

[28] Ioannidis JP. Interpretation of tests of heterogeneity and bias in meta-analysis. J Eval Clin Pract 2008;14:951–7.

[29] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.

[30] Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. J Clin Epidemiol 2008;61:991–6.

[31] Dechartres A, Boutron I, Trinquart L, Charles P, Ravaud P. Single-center trials show larger treatment effects than multicenter trials: evidence from a meta-epidemiologic study. Ann Intern Med 2011;155:39–51.

[32] Savović J, Jones H, Altman D, et al. Influence of reported study design characteristics on intervention effect estimates from randomised controlled trials: combined analysis of meta-epidemiological studies. Health Technol Assess 2012;16:1–82.

[33] Dechartres A, Trinquart L, Boutron I, Ravaud P. Influence of trial sample size on treatment effect estimates: meta-epidemiological study. BMJ 2013;346:f2304.

[34] Papageorgiou SN, Koretsi V, Jäger A. Bias from historical control groups used in orthodontic research: a meta-epidemiological study. Eur J Orthod 2017;39:98–105.

[35] Wallach JD, Sullivan PG, Trepanowski JF, Steyerberg EW, Ioannidis JP. Sex based subgroup differences in randomized controlled trials: empirical evidence from Cochrane meta-analyses. BMJ 2016;355:i5826.

[36] Papageorgiou SN, Höchli D, Eliades T. Outcomes of comprehensive fixed appliance orthodontic treatment: A systematic review with meta-analysis and methodological overview. Korean J Orthod 2017;47:401–413.

[37] Ioannidis JP, Greenland S, Hlatky MA, et al. Increasing value and reducing waste in research design, conduct, and analysis. Lancet 2014;383:166–75.

[38] Papageorgiou SN. Meta-analysis for orthodontists: Part II--Is all that glitters gold? J Orthod 2014;41:327–36.

[39] Pandis N, Shamseer L, Kokich VG, Fleming PS, Moher D. Active implementation strategy of CONSORT adherence by a dental specialty journal improved randomized clinical trial reporting. J Clin Epidemiol 2014;67:1044–8.

[40] Pandis N, Polychronopoulou A, Eliades T. An assessment of quality characteristics of randomised control trials published in dental journals. J Dent 2010;38:713–21.

[41] Hopewell S, Altman DG, Moher D, Schulz KF. Endorsement of the CONSORT Statement by high impact factor medical journals: a survey of journal editors and journal 'Instructions to Authors'. Trials 2008;9:20.

Figure Legends

Fig. 1. Flowdiagram for the identification and selection of studies in this meta-epidemiological study.

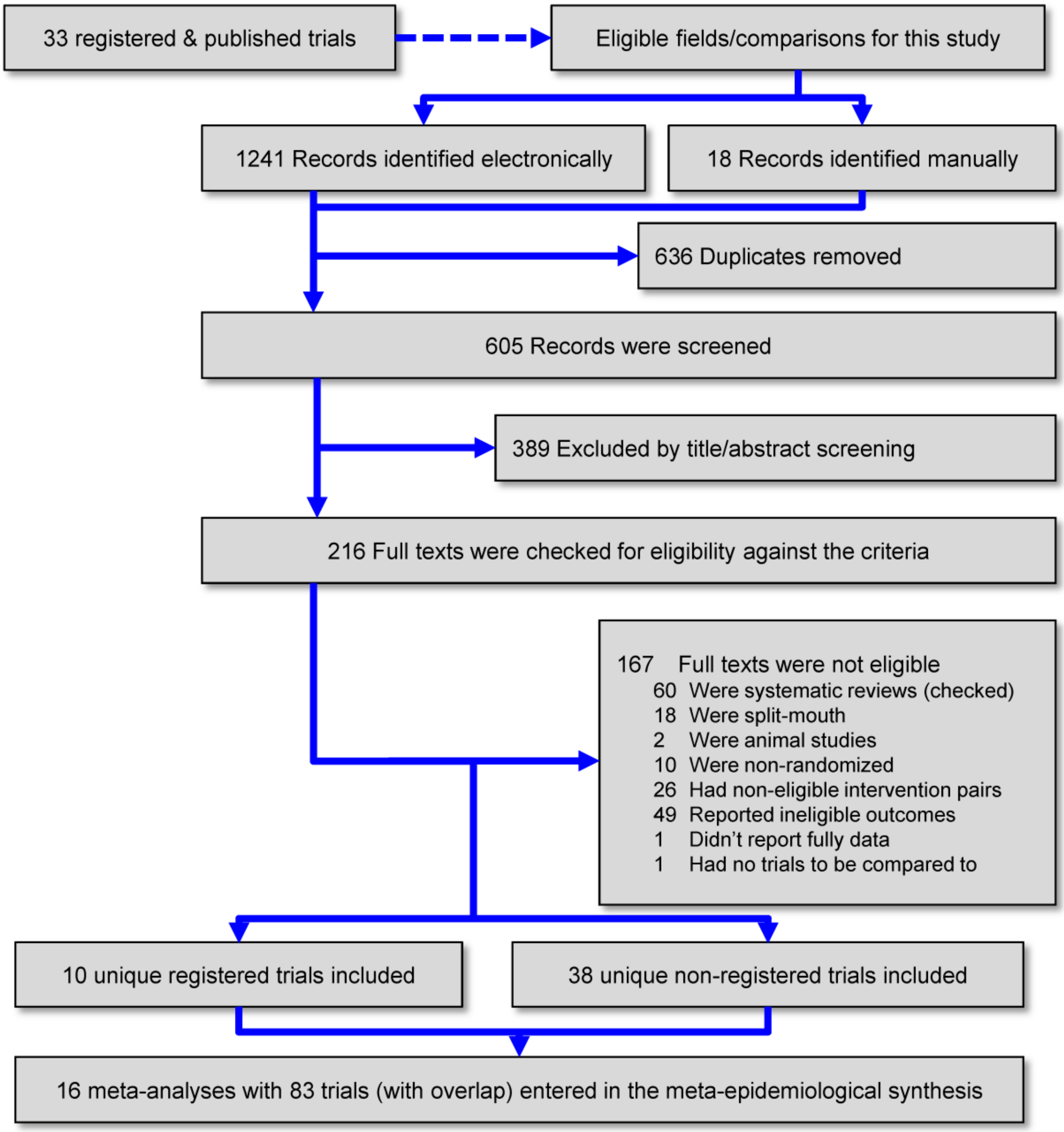


Fig. 2. Contour-enhanced forest plot for the meta-epidemiological synthesis using a Paule-Mandel random-effects model. Results are given as ΔSMDs and their 95% CIs. ΔSMD, standardized mean difference; CI, confidence intervals.

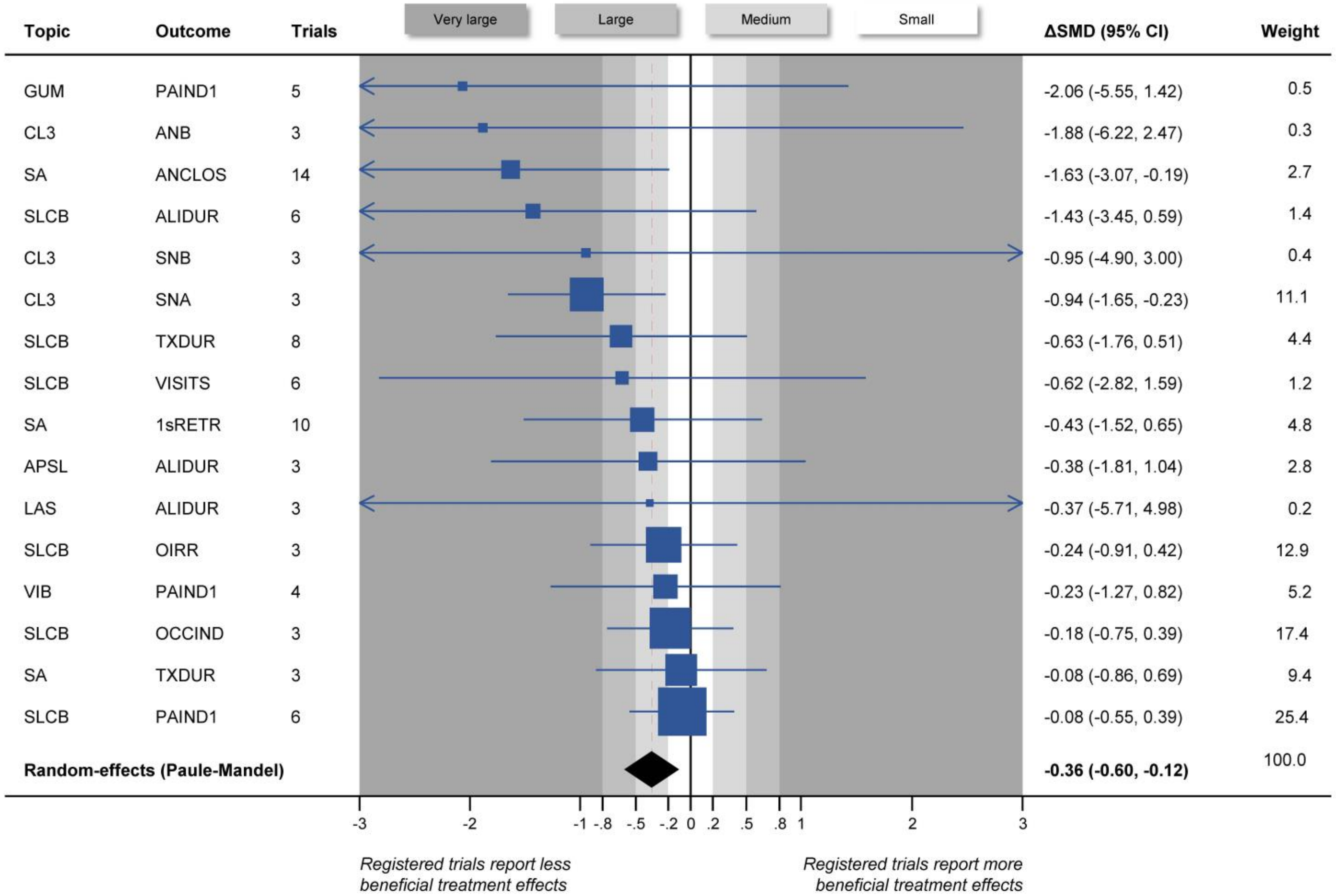


Fig. 3. Contour-enhanced funnel plot plot summarizing for the meta-epidemiological synthesis. ΔSMD, standardized mean difference.

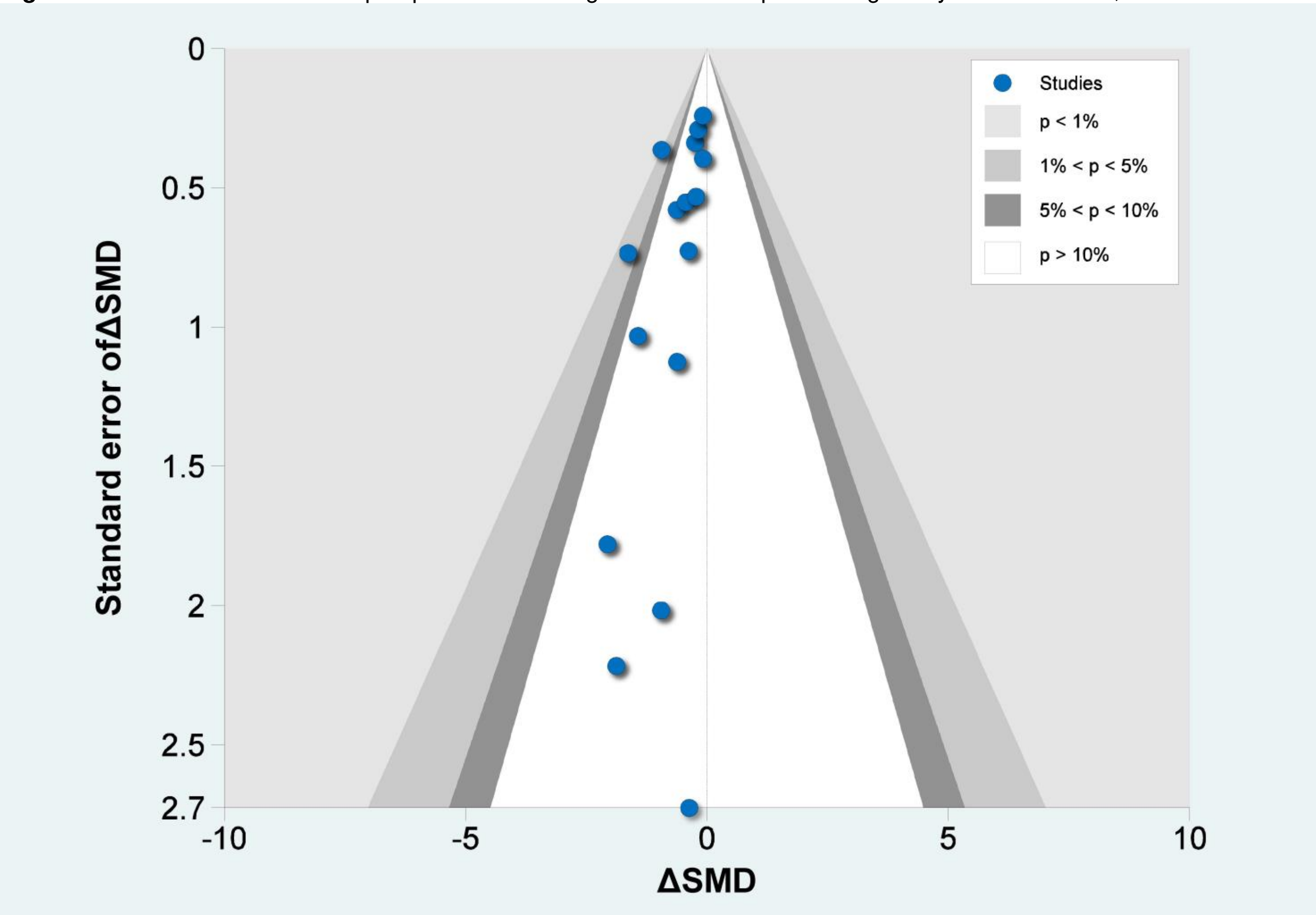


Table 1. Mixed-effects subgroup analyses of the meta-epidemiological synthesis. Negative effects indicate that registered trials show less beneficial treatment effects.

Factor	Category	Meta-analyses	ΔSMD (95% CI)	P*
Clinical scenario	Active vs passive self-ligating brackets for comprehensive treatment	1	-0.38 (-1.81,1.04)	0.39
	Maxillary protraction vs untreated control for maxillary deficiency	3	-0.96 (-1.66,-0.27)	
	Chewing gum vs no chewing gum for comprehensive treatment	1	-2.06 (-5.55,1.42)	
	Light therapy versus no light therapy for comprehensive treatment	1	-0.37 (-5.71,4.98)	
	Temporary anchorage devices vs conventional anchorage for anchorage reinforcement during extraction treatment	3	-0.56 (-1.40,0.29)	
	Self-ligating brackets vs conventional brackets for comprehensive treatment	6	-0.22 (-0.52,0.08)	
	Vibration adjuncts vs no vibration adjuncts for comprehensive treatment	1	-0.23 (-1.27,0.82)	
Outcome scope	Treatment efficacy	12	-0.51 (-0.83,-0.19)	0.11
	Adverse effects	4	-0.17 (-0.53,0.19)	
Outcome nature	Objective	13	-0.46 (-0.75,-0.17)	0.15
	Subjective (patient reported pain)	3	-0.14 (-0.56,0.29)	
Outcome direction[a]	Negative is favorable intervention effect	12	-0.29 (-0.59,-0.00)	0.40
	Positive is favorable intervention effect	4	-0.49 (-0.90,-0.07)	

Abbreviations: ΔSMD, difference in standardized mean differences; CI, confidence interval.
[a] this pertains to initial direction of outcome. Outcomes were uniformly transformed on the same direction to pool.
* for between-subgroup differences.

Table 2. Sensitivity analyses of the meta-epidemiological synthesis. Negative effects indicate that registered trials show less beneficial treatment effects.

Analysis	**Meta-analyses**	**ΔSMD (95% CI)**	**P**
Original analysis	16	-0.36 (-0.60,-0.12)	0.003
(i) Fixed effect model	16	Same as original	
(ii) Only the largest meta-analysis of each Intervention-Control comparison included	7	-0.30 (-0.63,0.02)	0.06
(iii) 50% of meta-analyses with most included trials	8	-0.36 (-0.71,-0.00)	0.05
(iv) Meta-analyses with ≥ 10 included trials	2	-0.94 (-2.09,0.22)	0.11
(v) Analysis adjusted for risk of bias due to inadequate random sequence generation[a]	6	-0.37 (-0.79,0.05)	0.09
(vi) Analysis adjusted for risk of bias due to inadequate outcome blinding[b]	3	-1.80 (-3.54,-0.06)	0.04

Abbreviations: ΔSMD, difference in standardized mean differences; CI, confidence interval.

[a] Only meta-analyses with ≥5 trials were included in this. Both registration status and low (or unclear/high) risk of bias for random sequence generation were used within each meta-analysis to calculate ΔSMDs, which were afterwards pooled across meta-analyses.

[b] Only meta-analyses with outcomes that could be blinded were included. Both registration status and low (or unclear/high) risk of bias for blind outcome measurement were used within each meta-analysis to calculate ΔSMDs, which were afterwards pooled across meta-analyses.

Supplementary data

Supplementary data related to this article can be found at:

Supplementary Table 1 List of identified registered, completed, and published trials in orthdontics (from PMID 28777820).

Supplementary Table 2 Literature searches performed on 15 August 2017 for the identification of registered or unregistered trials and systematic reviews/meta-analyses thereof for each of the eligible fields.

Supplementary Table 3a List of included/excluded studies on the topic of self-ligating brackets.

Supplementary Table 3b List of included/excluded studies on the topic of vibration as adjunct.

Supplementary Table 3c List of included/excluded studies on the topic of piezocision.

Supplementary Table 3d List of included/excluded studies on the topic of maxillary protraction for maxillary deficiency.

Supplementary Table 3e List of included/excluded studies on the topic of skeletal anchorage for space closure.

Supplementary Table 3f List of included/excluded studies on the topic of gum as adjunct.

Supplementary Table 3g List of included/excluded studies on the topic of low level light therapy.

Supplementary Table 4 Communcations with trialists to request data.

Supplementary Table 5 Charecteristics of included trials.

Supplementary Table 6 Details of included meta-analyses.

Supplementary Figure Forest plots for meta-analyses included in meta-epidemiological synthesis.

Appendix Post hoc changes to the protocol.

Additional files

Supplementary Table 1. List of identified registered, completed, and published trials in orthdontics (from PMID 28777820).

No	Thematology	Trial ID	Title
1	Adhesives	ISRCTN76156631	Trial excluded from consideration (split-mouth)
2	Adjunct; light-therapy	NCT02568436 (A) NCT02209818 (B) NCT01490385 (C) NCT02337192 (D)	Trial A eligible for consideration Trial B excluded from consideration (split-mouth) Trial C excluded from consideration (split-mouth) Trial D excluded from consideration (related to decontamination-not treatment effects)
3	Adjunct; shockwave	NCT01695928	Trial excluded from consideration (only existing trial on the subject)
4	Adjunct; surgical orthodontics	NCT02590835	Trial eligible for consideration
5	Adjunct; vibration	NCT02314975	Trial eligible for consideration
6	Bactereamia	ISRCTN27557210	Trial excluded from consideration (split-mouth)
7	Canine retraction	NCT02332421	Trial excluded from consideration (split-mouth)
8	Class II	ISRCTN61138858 (A) ISRCTN26364810 (B) ISRCTN52655400 (C)	Trial A excluded from consideration (only existing trial comparing Twin Block to control) Trial B excluded from consideration (only existing trial comparing Twin Block to control) Trial C excluded from consideration (comparison of two interventions)
9	Class III	NCT00519415 (A) ISRCTN10014340 (B)	Trial A excluded from consideration (comparison of two separate appliances) Trial B eligible for consideration
10	Chewing gum	ISRCTN79884739	Trial eligible for consideration
11	Mouthwash; complementary medicine	NCT01637948	Trial excluded from consideration (only existing trial on the subject)
12	Orthognathic	ISRCTN38986023	Trial excluded from consideration (comparison of two interventions)
13	Retention; RME	NCT01770782	Trial excluded from consideration (comparison of two interventions)
14	Brackets; self-ligating	ISRCTN67900267 (A) ISRCTN51381850 (B) ISRCTN05296896 (C) ISRCTN66185030 (D)	Trial A eligible for consideration Trial B eligible for consideration Trial C eligible for consideration Trial D eligible for consideration
15	Space closure	ISRCTN05771195	Trial excluded from consideration (two different interventions appliances; only trial on subject)
16	TADs; reinforcement	ISRCTN24433142 (A) NCT00995436 (B)	Trial A eligible for consideration Trial B eligible for consideration
17	Caries prevention	NCT01657539 (A) NCT00681135 (B) NCT01768390 (C) NCT02357771 (D) NCT02154594 (E) NCT02525458 (F)	Trials A-F excluded from consideration (compare two different interventions and adjuncts not related to treatment acceleration as specified in protocol)
18	Caries treatment	NCT01329731 (A) NCT01059058 (B)	Trial A excluded from consideration (only existing trial with those outcomes on the subject Trial B excluded from consideration (only existing trial with those outcomes on the subject

Supplementary Table 2. Literature searches performed on 15 August 2017 for the identification of registered or unregistered trials and systematic reviews/meta-analyses thereof for each of the eligible fields.

Field	Database	Search	Hits
SLB	MEDLINE (via Pubmed)	orthodon* AND ("self-ligating" OR "self-ligated") AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	96
	Cochrane	Same as PubMed	49
	Web of Knowledge*	Same as PubMed	71
	Scopus*	Same as PubMed	83
VIB	MEDLINE (via Pubmed)	orthodon* AND (vibrat* OR Acceledent OR "Accele-Dent" OR Orthoaccel OR "Ortho-Accel" OR "tooth masseuse" OR propel OR VPro5 OR Excellerator) AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	30
	Cochrane	Same as PubMed	11
	Web of Knowledge*	Same as PubMed	13
	Scopus*	Same as PubMed	20
PZ	MEDLINE (via Pubmed)	orthodon* AND (piezocision OR piezotome OR corticotomy OR corticocision OR corticision) AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	42
	Cochrane	Same as PubMed	9
	Web of Knowledge*	Same as PubMed	20
	Scopus*	Same as PubMed	24
CL3	MEDLINE (via Pubmed)	"Class III" AND (protraction OR facemask OR Delaire OR "reverse headgear") AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	39
	Cochrane	Same as PubMed	20
	Web of Knowledge*	Same as PubMed	23
	Scopus*	Same as PubMed	33
SA	MEDLINE (via Pubmed)	orthodon* AND (miniscrew OR miniimplant OR onplant OR miniplate OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "temporary anchorage" OR "skeletal anchorage" OR "anchorage reinforcement") AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	127
	Cochrane	Same as PubMed	49
	Web of Knowledge*	Same as PubMed	89
	Scopus*	Same as PubMed	132
Gum	MEDLINE (via Pubmed)	orthodon* AND (chew* AND gum) AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	26
	Cochrane	Same as PubMed	14
	Web of Knowledge*	Same as PubMed	23
	Scopus*	Same as PubMed	14
LT	MEDLINE (via Pubmed)	orthodon* AND ("low level laser" OR "low-level laser" OR LLLT) AND (random* OR "systematic review" OR "meta-analysis" OR "meta-analyses")	95
	Cochrane	Same as PubMed	29
	Web of Knowledge*	Same as PubMed	25
	Scopus*	Same as PubMed	35

*Limit for Dentistry and related fields used for Web of Knowledge and Scopus.
CL3, maxillary protraction for Class III; LT, light therapy; PZ, piezocision; SA, skeletal anchorage for Class II; SLB, self-ligating brackets; VIB, vibration adjuncts for fixed appliance treatment.

Supplementary Table 3a. List of included/excluded studies on the topic of self-ligating brackets.

Nr.	Paper	Status
1	自锁托槽与传统托槽不拔牙矫治软硬组织及牙弓变化的对比研究 [Changes in dental arch and hard and soft tissue caused by the self-ligating bracket and conventional bracket with non-extraction treatment]. 周昱 ； 郑敏玲 ； 胡荣党 ； 温州医学院附属口腔医院正畸科,温州,325000. 口腔医学 ； 2012年 03期 (2012 / 07 / 03)， P154 - 157.簡體中文	Excluded; missing fulltext
2	Anand M, Turpin DL, Jumani KS, Spiekerman CF, Huang GJ. Retrospective investigation of the effects and efficiency of self-ligating and conventional brackets. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(1):67-75.	Excluded; screening of title
3	Chen M, Li ZM, Liu X, Cai B, Wang DW, Feng ZC. Differences of treatment outcomes between self-ligating brackets with microimplant and headgear anchorages in adults with bimaxillary protrusion. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;147(4):465-71.	Excluded; screening of title
4	Elayyan F, Silikas N, Bearn D. Ex vivo surface and mechanical properties of coated orthodontic archwires. Eur J Orthod. 2008;30(6):661-7.	Excluded; screening of title
5	Fleming PS, Springate SD, Chate RAC. Myths and realities in orthodontics. British Dental Journal. 2015;218(3):105-10.	Excluded; screening of title
6	Livas C, Delli K, Karapsias S, Pandis N, Ren YJ. Investigation of bacteremia induced by removal of orthodontic mini-implants. Eur J Orthod. 2014;36(1):16-21.	Excluded; screening of title
7	Reicheneder CA, Gedrange T, Lange A, Baumert U, Proff P. Shear and tensile bond strength comparison of various contemporary orthodontic adhesive systems: An in-vitro study. American Journal of Orthodontics and Dentofacial Orthopedics. 2009;135(4).	Excluded; screening of title
8	Savoldi F, Visconti L, Dalessandri D, Bonetti S, Tsoi JKH, Matinlinna JP, et al. In vitro evaluation of the influence of velocity on sliding resistance of stainless steel arch wires in a self-ligating orthodontic bracket. Orthod Craniofac Res. 2017;20(2):119-25.	Excluded; screening of title
9	Teng GYY, Liou EJW. Interdental Osteotomies Induce Regional Acceleratory Phenomenon and Accelerate Orthodontic Tooth Movement. Journal of Oral and Maxillofacial Surgery. 2014;72(1):19-29.	Excluded; screening of title
10	Miles P, Fisher E. Assessment of the changes in arch perimeter and irregularity in the mandibular arch during initial alignment with the AcceleDent Aura appliance vs no appliance in adolescents: A single-blind randomized clinical trial. American Journal of Orthodontics and Dentofacial Orthopedics. 2016;150(6):928-36.	Excluded; screening of title
11	Pandis N, Polychronopoulou A, Eliades T. Alleviation of mandibular anterior crowding with copper-nickel-titanium vs nickel-titanium wires: a double-blind randomized control trial. Am J Orthod Dentofacial Orthop. 2009;136(2):152 e1-7;discussion -3.	Excluded; screening of title
12	Shaughnessy T, Kantarci A, Kau CH, Skrenes D, Skrenes S, Ma D. Intraoral photobiomodulation-induced orthodontic tooth alignment: a preliminary study. Bmc Oral Health. 2016;16.	Excluded; screening of title
13	Araujo RC, Bichara LM, Araujo AM, Normando D. Debris and friction of self-ligating and conventional orthodontic brackets after clinical use. Angle Orthod. 2015;85(4):673-7.	Excluded; screening of abstract
14	Archambault A, Major TW, Carey JP, Heo G, Badawi H, Major PW. A comparison of torque expression between stainless steel, titanium molybdenum alloy, and copper nickel titanium wires in metallic self-ligating brackets. Angle Orthod. 2010;80(5):884-9.	Excluded; screening of abstract
15	Baka ZM, Basciftci FA, Arslan U. Effects of 2 bracket and ligation types on plaque retention: a quantitative microbiologic analysis with real-time polymerase chain reaction. Am J Orthod Dentofacial Orthop. 2013;144(2):260-7.	Excluded; screening of abstract
16	Buck T, Pellegrini P, Sauerwein R, Leo MC, Covell DA, Jr., Maier T, et al. Elastomeric-ligated vs self-ligating appliances: a pilot study examining microbial colonization and white spot lesion formation after 1 year of orthodontic treatment. Orthodontics (Chic). 2011;12(2):108-21.	Excluded; screening of abstract
17	Cardoso Mde A, Saraiva PP, Maltagliati LA, Rhoden FK, Costa CC, Normando D, et al. Alterations in plaque accumulation and gingival inflammation promoted by treatment with self-ligating and conventional orthodontic brackets. Dental Press J Orthod. 2015;20(2):35-41.	Excluded; screening of abstract
18	Chapman JL. Bond failure rates of two self-ligating brackets: a randomised clinical trial. Aust Orthod J. 2011;27(2):139-44.	Excluded; screening of abstract
19	da Costa Monini A, Junior LG, Martins RP, Vianna AP. Canine retraction and anchorage loss: self-ligating versus conventional brackets in a randomized split-mouth study. Angle Orthod. 2014;84(5):846-52.	Excluded; screening of abstract
20	Dalessandri D, Lazzaroni E, Migliorati M, Piancino MG, Tonni I, Bonetti S. Self-ligating fully customized lingual appliance and chair-time reduction: a typodont study followed by a randomized clinical trial. Eur J Orthod. 2013;35(6):758-65.	Excluded; screening of abstract
21	Deguchi T, Imai M, Sugawara Y, Ando R, Kushima K, Takano-Yamamoto T. Clinical evaluation of a low-friction attachment device during canine retraction. Angle Orthodontist. 2007;77(6):968-72.	Excluded; screening of abstract
22	do Nascimento L, Pithon MM, dos Santos RL, Freitas AOA, Alviano DS, Nojima LI, et al. Colonization of Streptococcus mutans on esthetic brackets: Self-ligating vs conventional. American Journal of Orthodontics and Dentofacial Orthopedics. 2013;143(4):S72-S7.	Excluded; screening of abstract
23	Dominguez A, Velasquez SA. Effect of low-level laser therapy on pain following activation of orthodontic final archwires: a randomized controlled clinical trial. Photomed Laser Surg. 2013;31(1):36-40.	Excluded; screening of abstract
24	Elekdag-Turk S, Cakmak F, Isci D, Turk T. 12-month self-ligating bracket failure rate with a self-etching primer. Angle Orthod. 2008;78(6):1095-100.	Excluded; screening of

		abstract
25	Folco AA, Benitez-Roge SC, Iglesias M, Calabrese D, Pelizardi C, Rosa A, et al. Gingival response in orthodontic patients: Comparative study between self-ligating and conventional brackets. Acta Odontol Latinoam. 2014;27(3):120-4.	Excluded; screening of abstract
26	Ireland AJ, Soro V, Sprague SV, Harradine NW, Day C, Al-Anezi S, et al. The effects of different orthodontic appliances upon microbial communities. Orthod Craniofac Res. 2014;17(2):115-23.	Excluded; screening of abstract
27	Kaygisiz E, Uzuner FD, Yuksel S, Taner L, Culhaoglu R, Sezgin Y, et al. Effects of self-ligating and conventional brackets on halitosis and periodontal conditions. Angle Orthod. 2015;85(3):468-73.	Excluded; screening of abstract
28	Li Y, Tang N, Xu ZR, Feng XX, Yang L, Zhao ZH. Bidimensional techniques for stronger anterior torque control in extraction cases A combined clinical and typodont study. Angle Orthodontist. 2012;82(4):715-22.	Excluded; screening of abstract
29	Sabrina, Krisnawati, Soegiharto BM. The comparison of space closure rate between conventional and passive self-ligating system using elastomeric chain in maxilla. Journal of International Dental and Medical Research. 2016;9(Specialissue):356-61.	Excluded; screening of abstract
30	Liu Y, Guo HM. [Comparison of root resorption between self-ligating and conventional brackets using cone-beam CT]. Shanghai Kou Qiang Yi Xue. 2016;25(2):238-41.	Excluded; screening of abstract
31	Major TW, Carey JP, Nobes DS, Heo G, Major PW. Mechanical effects of third-order movement in self-ligated brackets by the measurement of torque expression. Am J Orthod Dentofacial Orthop. 2011;139(1):e31-44.	Excluded; screening of abstract
32	Mezomo M, de Lima ES, de Menezes LM, Weissheimer A, Allgayer S. Maxillary canine retraction with self-ligating and conventional brackets. Angle Orthod. 2011;81(2):292-7.	Excluded; screening of abstract
33	Miles PG. Self-ligating vs conventional twin brackets during en-masse space closure with sliding mechanics. Am J Orthod Dentofacial Orthop. 2007;132(2):223-5.	Excluded; screening of abstract
34	Montasser MA, Keilig L, Bourauel C. Archwire diameter effect on tooth alignment with different bracket-archwire combinations. American Journal of Orthodontics and Dentofacial Orthopedics. 2016;149(1):76-83.	Excluded; screening of abstract
35	Mummolo S, Marchetti E, Giuca MR, Gallusi G, Tecco S, Gatto R, et al. In-office bacteria test for a microbial monitoring during the conventional and self-ligating orthodontic treatment. Head Face Med. 2013;9:7.	Excluded; screening of abstract
36	Nahas AZ, Samara SA, Rastegar-Lari TA. Decrowding of lower anterior segment with and without photobiomodulation: a single center, randomized clinical trial. Lasers Med Sci. 2017;32(1):129-35.	Excluded; screening of abstract
37	Nalcaci R, Ozat Y, Cokakoglu S, Turkkahraman H, Onal S, Kaya S. Effect of bracket type on halitosis, periodontal status, and microbial colonization. Angle Orthod. 2014;84(3):479-85.	Excluded; screening of abstract
38	Northrup RG, Berzins DW, Bradley TG, Schuckit W. Shear bond strength comparison between two orthodontic adhesives and self-ligating and conventional brackets. Angle Orthodontist. 2007;77(4):701-6.	Excluded; screening of abstract
39	Oz AA, Arici N, Arici S. The clinical and laboratory effects of bracket type during canine distalization with sliding mechanics. Angle Orthod. 2012;82(2):326-32.	Excluded; screening of abstract
40	Pandis N, Papaioannou W, Kontou E, Nakou M, Makou M, Eliades T. Salivary Streptococcus mutans levels in patients with conventional and self-ligating brackets. Eur J Orthod. 2010;32(1):94-9.	Excluded; screening of abstract
41	Pandis N, Polychronopoulou A, Eliades T. Failure rate of self-ligating and edgewise brackets bonded with conventional acid etching and a self-etching primer: a prospective in vivo study. Angle Orthod. 2006;76(1):119-22.	Excluded; screening of abstract
42	Pejda S, Varga ML, Milosevic SA, Mestrovic S, Slaj M, Repic D, et al. Clinical and microbiological parameters in patients with self-ligating and conventional brackets during early phase of orthodontic treatment. Angle Orthod. 2013;83(1):133-9.	Excluded; screening of abstract
43	Pellegrini P, Sauerwein R, Finlayson T, McLeod J, Covell DA, Jr., Maier T, et al. Plaque retention by self-ligating vs elastomeric orthodontic brackets: quantitative comparison of oral bacteria and detection with adenosine triphosphate-driven bioluminescence. Am J Orthod Dentofacial Orthop. 2009;135(4):426 e1-9; discussion -7.	Excluded; screening of abstract
44	Polat O, Gokcelik A, Arman A, Arhun N. A comparison of white spot lesion formation between a self-ligating bracket and a conventional preadjusted straight wire bracket. World J Orthod. 2008;9(2):e46-50.	Excluded; screening of abstract
45	Sahoo N, Kailasam V, Padmanabhan S, Chitharanjan AB. In-vivo evaluation of salivary nickel and chromium levels in conventional and self-ligating brackets. Am J Orthod Dentofacial Orthop. 2011;140(3):340-5.	Excluded; screening of abstract
46	Scribante A, Sfondrini MF, Gatti S, Gandini P. Disinclusion of unerupted teeth by mean of self-ligating brackets: Effect of blood contamination on shear bond strength. Medicina Oral Patologia Oral Y Cirugia Bucal. 2013;18(1):E162-E7.	Excluded; screening of abstract
47	Uzuner FD, Kaygisiz E, Cankaya ZT. Effect of the bracket types on microbial colonization and periodontal status. Angle Orthod. 2014;84(6):1062-7.	Excluded; screening of abstract
48	Wong H, Collins J, Tinsley D, Sandler J, Benson P. Does the bracket-ligature combination affect the amount of orthodontic space closure over three months? A randomized controlled trial. J Orthod.	Excluded; screening of

	2013;40(2):155-62.	abstract
49	Atik E, Ciger S. An assessment of conventional and self-ligating brackets in Class I maxillary constriction patients. Angle Orthod. 2014;84(4):615-22.	Excluded; not relevant
50	Keith DJ, Rinchuse DJ, Kennedy M, Zullo T. Effect of text message follow-up on patient's self-reported level of pain and anxiety. Angle Orthod. 2013;83(4):605-10.	Excluded; not relevant
51	Rinchuse DJ. Developmental occlusion, orthodontic interventions, and orthognathic surgery for adolescents. Dental Clinics of North America. 2006;50(1):69-86.	Excluded; not relevant
52	Lombardo L. Ectopic canine control with conventional brackets. Int Orthod. 2012;10(4):377-403.	Excluded; not relevant
53	Tsichlaki A, Chin SY, Pandis N, Fleming PS. How long does treatment with fixed orthodontic appliances last? A systematic review. American Journal of Orthodontics and Dentofacial Orthopedics. 2016;149(3):308-18.	Excluded; not relevant
54	Zhang DP, Liu J, Liu Y, Sun N, Yi JC. [Influence of self-ligating and conventional brackets on dental arch width in non-extraction treatment: a meta analysis]. Shanghai Kou Qiang Yi Xue. 2014;23(3):367-72.	Excluded; not relevant
55	Burrow SJ, Proffit WR, Keim RG. Drs. S.J. "Jack" Burrow and William R. Proffit on the efficacy of self-ligating brackets. J Clin Orthod. 2013;47(7):413-8.	Excluded; no clinical study
56	Sfondrini MF, Scribante A, Gatti S, Di Nicola P, Piacentini C. Effects of blood contamination on the detachment of three different types of self-ligating brackets: An in vitro study. Mondo Ortodontico. 2011;36(5):196-203.	Excluded; no clinical study
57	Higa RH, Henriques JFC, Janson G, Matias M, de Freitas KMS, Henriques FP, et al. Force level of small diameter nickel-titanium orthodontic wires ligated with different methods. Prog Orthod. 2017;18(1):21.	Excluded; no clinical study
58	O'Brien K. Longer treatment times with self-ligated orthodontic brackets. Evid Based Dent. 2014;15(3):92.	Excluded; no clinical study
59	Nainan O, Mitra R, Chopra SS. Re: Maxillary canine retraction with self-ligating and conventional brackets. A randomized clinical trial. By: Mauri cio Mezomo; Eduardo S. de Lima; Luciane Macedo de Menezes; Andre' Weissheimer; Susiane Allgayer. Angle Orthod. 2011;81:292-297. Angle Orthod. 2011;81(5):926-7; author reply 7.	Excluded; no clinical study
60	Fleming PS, DiBiase AT, Lee RT. Self-ligating appliances: evolution or revolution? Aust Orthod J. 2008;24(1):41-9.	Excluded; no clinical study
61	Marshall SD, Currier GF, Hatch NE, Huang GJ, Nah HD, Owens SE, et al. Self-ligating bracket claims. American Journal of Orthodontics and Dentofacial Orthopedics. 2010;138(2):128-31.	Excluded; no clinical study
62	Fleming PS, O'Brien K. Self-ligating brackets do not increase treatment efficiency. American Journal of Orthodontics and Dentofacial Orthopedics. 2013;143(1):11-9.	Excluded; no clinical study
63	Harradine N. Self-ligating brackets increase treatment efficiency. American Journal of Orthodontics and Dentofacial Orthopedics. 2013;143(1):10-8.	Excluded; no clinical study
64	Shin K. Self-ligating Brackets May Not Have Clinical Advantages Over Conventional Brackets for the Periodontal Health of Adolescent Orthodontic Patients. J Evid Based Dent Pract. 2017;17(2):102-4.	Excluded; no clinical study
65	Kaklamanos EG, Athanasiou AE. Systematic review of self-ligating brackets. Am J Orthod Dentofacial Orthop. 2011;139(2):145-6; author reply 6-7.	Excluded; no clinical study
66	Pandis N, Fleming PS, Spineli LM, Salanti G. Initial orthodontic alignment effectiveness with self-ligating and conventional appliances: A network meta-analysis in practice. American Journal of Orthodontics and Dentofacial Orthopedics. 2014;145(4):S152-S63.	Excluded; no clinical study
67	Archambault A, Lacoursiere R, Badawi H, Major PW, Carey J, Flores-Mir C. Torque Expression in Stainless Steel Orthodontic Brackets. Angle Orthodontist. 2010;80(1):201-10.	Excluded; no clinical study
68	Machibya FM, Bao XF, Zhao LH, Hu M. Treatment time, outcome, and anchorage loss comparisons of self-ligating and conventional brackets. Angle Orthodontist. 2013;83(2):280-5.	Excluded; no randomisation
69	Pandis N, Polychronopoulou A, Eliades T. Self-ligating vs conventional brackets in the treatment of mandibular crowding: a prospective clinical trial of treatment duration and dental effects. Am J Orthod Dentofacial Orthop. 2007;132(2):208-15.	Excluded; no randomisation
70	Pandis N, Strigou S, Eliades T. Maxillary incisor torque with conventional and self-ligating brackets: a prospective clinical trial. Orthod Craniofac Res. 2006;9(4):193-8.	Excluded; no randomisation
71	Birdsall J, Hunt NP, Sabbah W, Moseley HC. Accuracy of positioning three types of self-ligating brackets compared with a conventionally ligating bracket. J Orthod. 2012;39(1):34-42.	Excluded; no randomisation
72	Bertl MH, Onodera K, Celar AG. A prospective randomized split-mouth study on pain experience during chairside archwire manipulation in self-ligating and conventional brackets. Angle Orthod. 2013;83(2):292-7.	Excluded; split-mouth study
73	Celar AG, Onodera K, Bertl MH, Astl E, Bantleon HP, Sato S, et al. Geometric morphometric evaluations of a randomized prospective split-mouth study on modes of ligation and reverse-curve mechanics. Orthod Craniofac Res. 2014;17(3):158-69.	Excluded; split-mouth study
74	Hassan SE, Hajeer MY, Alali OH, Kaddah AS. The Effect of Using Self-ligating Brackets on Maxillary Canine Retraction: A Split-mouth Design Randomized Controlled Trial. J Contemp Dent Pract. 2016;17(6):496-503.	Excluded; split-mouth study
75	Cattaneo PM, Salih RA, Melsen B. Labio-lingual root control of lower anterior teeth and canines obtained by active and passive self-ligating brackets. Angle Orthod. 2013;83(4):691-7.	Excluded; non-eligible outcome
76	de Almeida MR, Herrero F, Fattal A, Davoody AR, Nanda R, Uribe F. A comparative anchorage control study between conventional and self-ligating bracket systems using differential moments. Angle Orthodontist. 2013;83(6):937-42.	Excluded; non-eligible outcome
77	Ireland AJ, Songra G, Clover M, Atack NE, Sherriff M, Sandy JR. Effect of gender and Frankfort mandibular plane angle on orthodontic space closure: A randomized controlled trial. Orthodontics and Craniofacial Research. 2016;19(2):74-82.	Excluded; non-eligible outcome

78	Kohli SS, Kohli VS. Patient pain experience after placement of initial aligning archwire using active and passive self-ligating bracket systems: a randomized clinical trial. Orthodontics (Chic) [Internet]. 2012; (1):[e58-65.	Excluded; non-eligible outcome
79	Leite V, Conti AC, Navarro R, Almeida M, Oltramari-Navarro P, Almeida R. Comparison of root resorption between self-ligating and conventional preadjusted brackets using cone beam computed tomography. Angle Orthodontist. 2012;82(6):1078-82.	Excluded; non-eligible outcome
80	Othman SA, Mansor N, Saub R. Randomized controlled clinical trial of oral health-related quality of life in patients wearing conventional and self-ligating brackets. Korean Journal of Orthodontics. 2014;44(4):168-76.	Excluded; non-eligible outcome
81	Ab Rahman N, Wey MC, Othman SA. Mandibular arch orthodontic treatment stability using passive self-ligating and conventional systems in adults: A randomized controlled trial. Korean Journal of Orthodontics. 2017;47(1):11-20.	Excluded; non-eligible outcome
82	Jayachandran B, Padmanabhan R, Vijayalakshmi D, Padmanabhan J. Comparative evaluation of efficacy of self-ligating interactive bracket with conventional preadjusted bracket: A clinical study. Contemp Clin Dent. 2016;7(2):158-62.	Excluded; non-eligible outcome
83	Al-Anezi SA. Dental plaque associated with self-ligating brackets during the initial phase of orthodontic treatment: A 3-month preliminary study. J Orthod Sci. 2014;3(1):7-11.	Excluded; non-eligible outcome
84	Ehsani S, Mandich MA, El-Bialy TH, Flores-Mir C. Frictional resistance in self-ligating orthodontic brackets and conventionally ligated brackets. A systematic review. Angle Orthod. 2009;79(3):592-601.	Excluded; non-eligible outcome
85	Mezomo M, de Lima ES, de Menezes LM, Weissheimer A, Allgayer S. Maxillary canine retraction with self-ligating and conventional brackets A randomized clinical trial. Angle Orthodontist. 2011;81(2):292-7.	Excluded; non-eligible outcome
86	Lai TT, Chiou JY, Lai TC, Chen T, Chen MH. Oral health-related quality of life in orthodontic patients during initial therapy with conventional brackets or self-ligating brackets. Journal of Dental Sciences. 2017;12(2):161-72.	Excluded; non-eligible outcome
87	Al-Thomali Y, Mohamed RN, Basha S. Torque expression in self-ligating orthodontic brackets and conventionally ligated brackets: A systematic review. J Clin Exp Dent. 2017;9(1):e123-e8.	Systematic review; checked for eligible trials
88	Arnold S, Koletsi D, Patcas R, Eliades T. The effect of bracket ligation on the periodontal status of adolescents undergoing orthodontic treatment. A systematic review and meta-analysis. J Dent. 2016;54:13-24.	Systematic review; checked for eligible trials
89	do Nascimento LE, de Souza MM, Azevedo AR, Maia LC. Are self-ligating brackets related to less formation of Streptococcus mutans colonies? A systematic review. Dental Press J Orthod. 2014;19(1):60-8.	Systematic review; checked for eligible trials
90	Celar A, Schedlberger M, Dorfler P, Bertl M. Systematic review on self-ligating vs conventional brackets: initial pain, number of visits, treatment time. Journal of Orofacial Orthopedics 2013; 1:40-51.	Systematic review; checked for eligible trials
91	Chen SS, Greenlee GM, Kim JE, Smith CL, Huang GJ. Systematic review of self-ligating brackets (Provisional abstract). American Journal of Orthodontics and Dentofacial Orthopedics 2010; (6):726.e1-.e18.	Systematic review; checked for eligible trials
92	Fleming PS, Johal A. Self-ligating brackets in orthodontics. A systematic review. Angle Orthod. 2010;80(3):575-84.	Systematic review; checked for eligible trials
93	Kalemaj Z, Debernardl CL, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: A systematic review. European Journal of Oral Implantology. 2015;8(1):9-24.	Systematic review; checked for eligible trials
94	Papageorgiou SN, Konstantinidis I, Papadopoulou K, Jager A, Bourauel C. Clinical effects of pre-adjusted edgewise orthodontic brackets: a systematic review and meta-analysis. Eur J Orthod. 2014;36(3):350-63.	Systematic review; checked for eligible trials
95	Yang X, Su N, Shi Z, Xiang Z, He Y, Han X, et al. Effects of self-ligating brackets on oral hygiene and discomfort: a systematic review and meta-analysis of randomized controlled clinical trials. Int J Dent Hyg. 2017;15(1):16-22.	Systematic review; checked for eligible trials
96	Yang XR, He YR, Chen T, Zhao MY, Yan YQ, Wang HZ, et al. Differences between active and passive self-ligating brackets for orthodontic treatment. Journal of Orofacial Orthopedics-Fortschritte Der Kieferorthopadie. 2017;78(2):121-8.	Systematic review; checked for eligible trials
97	Yi J, Li M, Li Y, Li X, Zhao Z. Root resorption during orthodontic treatment with self-ligating or conventional brackets: a systematic review and meta-analysis. Bmc Oral Health. 2016;16(1):125.	Systematic review; checked for eligible trials
98	Zhou Q, Ul Haq AA, Tian L, Chen X, Huang K, Zhou Y. Canine retraction and anchorage loss self-ligating versus conventional brackets: a systematic review and meta-analysis. Bmc Oral Health. 2015;15(1):136.	Systematic review; checked for eligible trials
99	Almeida MR, Futagami C, Conti AC, Oltramari-Navarro PV, Navarro Rde L. Dentoalveolar mandibular changes with self-ligating versus conventional bracket systems: A CBCT and dental cast study. Dental Press J Orthod. 2015;20(3):50-7.	Included for potential evaluation
100	Bhardwaj P, Sonar S, Batra P. Alignment efficiency of standard versus tandem wire mechanics using conventional and self-ligating brackets: A pilot study. J Indian Orthod Soc 2017;51:103-9.	Included for potential evaluation
101	Bhatia V, Kalha AS, Nanda SB. An Evaluation of Smart Clip Self-Ligating Bracket System: Comparison of Treatment Outcome and Patient Response between Self-ligating and Conventional Pre-adjusted Edgewise Appliance. Orthod J Nepal 2014;4(2):12-15	Included for potential evaluation
102	Cattaneo PM, Treccani M, Carlsson K, Thorgeirsson T, Myrda A, Cevidanes LH, et al. Transversal maxillary dento-alveolar changes in patients treated with active and passive self-ligating brackets: a	Included for potential

	randomized clinical trial using CBCT-scans and digital models. Orthod Craniofac Res. 2011;14(4):222-33.	evaluation
103	Celikoglu M, Bayram M, Nur M, Kilkis D. Mandibular changes during initial alignment with SmartClip self-ligating and conventional brackets: A single-center prospective randomized controlled clinical trial. Korean Journal of Orthodontics. 2015;45(2):89-94.	Included for potential evaluation
104	Chen XH, Hua YM, Xie XQ, Yu XJ, Wang J, Liu LM. [Clinical study of extraction treatment of Class II division I malocclusion with Empower self-ligating brackets]. Shanghai Kou Qiang Yi Xue. 2013;22(3):316-21.	Included for potential evaluation
105	DiBiase AT, Nasr IH, Scott P, Cobourne MT. Duration of treatment and occlusal outcome using Damon3 self-ligated and conventional orthodontic bracket systems in extraction patients: a prospective randomized clinical trial. Am J Orthod Dentofacial Orthop. 2011;139(2):e111-6.	Included for potential evaluation
106	Fleming PS, DiBiase AT, Lee RT. Randomized clinical trial of orthodontic treatment efficiency with self-ligating and conventional fixed orthodontic appliances. Am J Orthod Dentofacial Orthop. 2010;137(6):738-42.	Included for potential evaluation
107	Fleming PS, DiBiase AT, Sarri G, Lee RT. Comparison of mandibular arch changes during alignment and leveling with 2 preadjusted edgewise appliances. Am J Orthod Dentofacial Orthop. 2009a;136(3):340-7.	Included for potential evaluation
108	Fleming PS, DiBiase AT, Sarri G, Lee RT. Efficiency of mandibular arch alignment with 2 preadjusted edgewise appliances. Am J Orthod Dentofacial Orthop. 2009b;135(5):597-602.	Included for potential evaluation
109	Fleming PS, Dibiase AT, Sarri G, Lee RT. Pain experience during initial alignment with a self-ligating and a conventional fixed orthodontic appliance system. A randomized controlled clinical trial. Angle Orthod. 2009c;79(1):46-50.	Included for potential evaluation
110	Fleming PS, Lee RT, Marinho V, Johal A. Comparison of maxillary arch dimensional changes with passive and active self-ligation and conventional brackets in the permanent dentition: a multicenter, randomized controlled trial. Am J Orthod Dentofacial Orthop. 2013 Aug;144(2):185-93.	Included for potential evaluation
111	Fleming PS, Lee RT, McDonald T, Pandis N, Johal A. The timing of significant arch dimensional changes with fixed orthodontic appliances: data from a multicenter randomised controlled trial. J Dent. 2014;42(1):1-6.	Included for potential evaluation
112	Gaspar-Ribeiro DA, de Almeida MR, Conti AC, Navarro R, Oltramari-Navarro P, Almeida R, Fernandes T. Efficiency of mandibular arch alignment with self-ligating and conventional edgewise appliances: a dental cast study. Dentistry. 2012;2:128.	Included for potential evaluation
113	Ibiapina DJ, Oltramari-Navarro PV, Navarro RL, Almeida MR, Mendonça DL, Conti ACCF. Assessment of Dental Arch Changes and Buccal Bone Thickness in Patients treated with Self-ligating Brackets. J Contemp Dent Pract 2016;17(6):434-439.	Included for potential evaluation
114	Jiang LQ, Dai J, Liu JL. Comparative study on pain experience with fixed orthodontic treatment of Damon 3Mx™ self-ligating and conventional Mbt™ appliance. J Xi'an Jiaotong University (Medical Sciences) 2009;30:648–650.	Included for potential evaluation
115	Johansson K, Lundstrom F. Orthodontic treatment efficiency with self-ligating and conventional edgewise twin brackets: a prospective randomized clinical trial. Angle Orthod. 2012;82(5):929-34.	Included for potential evaluation
116	Kaklamanos EG, Mavreas D, Tsalikis L, Karagiannis V, Athanasiou AE. Treatment duration and gingival inflammation in Angle's Class I malocclusion patients treated with the conventional straight-wire method and the Damon technique: a single-centre, randomised clinical trial. J Orthod. 2017 Jun;44(2):75-81.	Included for potential evaluation
117	Kalemaj Z, Buti J, Deregibus A, Canuto RM, Maggiora M, Debernardi CL. Aligning Effectiveness, Secretion of Interleukin 1β and Pain Control During Fixed Orthodontic Treatment with Self-Ligating Appliances and Supplemental Vibrational Appliances. A Randomized Controlled Clinical Trial. J Biomed 2017; 2(1):25-33.	Included for potential evaluation
118	Miles P, Weyant R. Porcelain brackets during initial alignment: are self-ligating cosmetic brackets more efficient? Aust Orthod J. 2010;26(1):21-6.	Included for potential evaluation
119	O'Dywer L, Littlewood SJ, Rahman S, Spencer RJ, Barber SK, Russell JS. A multi-center randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 1: Treatment efficiency. Angle Orthodontist. 2016;86(1):142-8.	Included for potential evaluation
120	Pandis N, Polychronopoulou A, Eliades T. Active or passive self-ligating brackets? A randomized controlled trial of comparative efficiency in resolving maxillary anterior crowding in adolescents. Am J Orthod Dentofacial Orthop. 2010;137(1):12 e1-6; discussion -3.	Included for potential evaluation
121	Pandis N, Polychronopoulou A, Katsaros C, Eliades T. Comparative assessment of conventional and self-ligating appliances on the effect of mandibular intermolar distance in adolescent nonextraction patients: a single-center randomized controlled trial. Am J Orthod Dentofacial Orthop. 2011;140(3):e99-e105.	Included for potential evaluation
122	Pringle AM, Petrie A, Cunningham SJ, McKnight M. Prospective randomized clinical trial to compare pain levels associated with 2 orthodontic fixed bracket systems. Am J Orthod Dentofacial Orthop. 2009;136(2):160-7.	Included for potential evaluation
123	Rahman S, Spencer RJ, Littlewood SJ, O'Dywer L, Barber SK, Russell JS. A multicenter randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 2: Pain perception. Angle Orthodontist. 2016;86(1):149-56.	Included for potential evaluation
124	Reddy VB, Kumar TA, Prasad M, Nuvvula S, Patil RG, Reddy PK. A comparative in vivo evaluation of the alignment efficiency of 5 ligation methods: a prospective randomized clinical trial. Eur J Dent. 2014;8:23–31.	Included for potential evaluation
125	Scott P, DiBiase AT, Sherriff M, Cobourne MT. Alignment efficiency of Damon3 self-ligating and conventional orthodontic bracket systems: a randomized clinical trial. Am J Orthod Dentofacial	Included for potential

	Orthop. 2008a;134(4):470 e1-8.	evaluation
126	Scott P, Sherriff M, Dibiase AT, Cobourne MT. Perception of discomfort during initial orthodontic tooth alignment using a self-ligating or conventional bracket system: a randomized clinical trial. Eur J Orthod. 2008b;30(3):227-32.	Included for potential evaluation
127	Songra G, Clover M, Atack NE, Ewings P, Sherriff M, Sandy JR, et al. Comparative assessment of alignment efficiency and space closure of active and passive self-ligating vs conventional appliances in adolescents: a single-center randomized controlled trial. Am J Orthod Dentofacial Orthop. 2014;145(5):569-78.	Included for potential evaluation
128	Uzdil F. Comparison of effectiveness of different low friction bracket systems and conventional brackets in the leveling phase. Doctoral thesis, 2008, Çukurova University	Included for potential evaluation
129	Wahab RM, Idris H, Yacob H, Ariffin SH. Comparison of self- and conventional-ligating brackets in the alignment stage. Eur J Orthod. 2012;34(2):176-81.	Included for potential evaluation

Supplementary Table 3b. List of included/excluded studies on the topic of vibration as adjunct.

Nr	Paper	Status
1	Son S, Motoyoshi M, Uchida Y, Shimizu N. Comparative study of the primary stability of self-drilling and self-tapping orthodontic miniscrews. Am J Orthod Dentofacial Orthop. 2014;145(4):480-5.	Excluded; screening of title
2	Erratum to: Non-Orthodontic Abstracts (Journal of Orthodontics, (2016), 43, 3, (243-245), 10.1080/14653125.2016.1143233). Journal of Orthodontics. 2017;44(1):74.	Excluded; screening of title
3	Carney LO, Campbell PM, Spears R, Ceen RF, Melo AC, Buschang PH. Effects of pilot holes on longitudinal miniscrew stability and bony adaptation. American Journal of Orthodontics and Dentofacial Orthopedics. 2014;146(5):554-64.	Excluded; screening of title
4	Cuairán C, Campbell PM, Kontogiorgos E, Taylor RW, Melo AC, Buschang PH. Local application of zoledronate enhances miniscrew implant stability in dogs. American Journal of Orthodontics and Dentofacial Orthopedics. 2014;145(6):737-49.	Excluded; screening of title
5	Ure DS, Oliver DR, Kim KB, Melo AC, Buschang PH. Stability changes of miniscrew implants over time A pilot resonance frequency analysis. Angle Orthodontist. 2011;81(6):994-1000.	Excluded; screening of title
6	Uysal T, Ekizer A, Akcay H, Etoz O, Guray E. Resonance frequency analysis of orthodontic miniscrews subjected to light-emitting diode photobiomodulation therapy. European Journal of Orthodontics. 2012;34(1):44-51.	Excluded; screening of title
7	Yadav S, Assefnia A, Gupta H, Vishwanath M, Kalajzic Z, Allareddy V, et al. The effect of low-frequency mechanical vibration on retention in an orthodontic relapse model. European Journal of Orthodontics. 2016;38(1):44-50.	Excluded; screening of title
8	Darendeliler MA, Zea A, Shen G, Zoellner H. Effects of pulsed electromagnetic field vibration on tooth movement induced by magnetic and mechanical forces: a preliminary study. Australian Dental Journal. 2007;52(4):282-7.	Excluded; screening of abstract
9	Yadav S, Dobie T, Assefnia A, Gupta H, Kalajzic Z, Nanda R. Effect of low-frequency mechanical vibration on orthodontic tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(3):440-9.	Excluded; screening of abstract
10	Yadav S, Dobie T, Assefnia A, Kalajzic Z, Nanda R. The effect of mechanical vibration on orthodontically induced root resorption. Angle Orthodontist. 2016;86(5):740-5.	Excluded; screening of abstract
11	Zhang CC, Li J, Zhang LK, Zhou Y, Hou WW, Quan HX, et al. Effects of mechanical vibration on proliferation and osteogenic differentiation of human periodontal ligament stem cells. Archives of Oral Biology. 2012;57(10):1395-407.	Excluded; screening of abstract
12	Alikhani M, Khoo E, Alyami B, Raptis M, Salgueiro JM, Oliveira SM, et al. Osteogenic effect of high-frequency acceleration on alveolar bone. J Dent Res. 2012;91(4):413-9.	Excluded; not relevant
13	Alikhani M, Lopez JA, Alabdullah H, Vongthongleur T, Sangsuwon C, Alansari S, et al. High-Frequency Acceleration: Therapeutic Tool to Preserve Bone following Tooth Extractions. J Dent Res. 2016;95(3):311-8.	Excluded; not relevant
14	Caldas SGFR, Ribeiro AA, Santos-Pinto LD, Martins LP, Matoso RM. The effectiveness of mandibular advancement intraoral appliances in the treatment of the snoring and obstructive sleep apnea and hypopnea syndrome (OSAHS): Systematic review. Revista Dental Press de Ortodontia e Ortopedia Facial. 2009;14(4):74-82.	Excluded; not relevant
15	Camacho AD, Velasquez Cujar SA. Dental movement acceleration: Literature review by an alternative scientific evidence method. World J Methodol. 2014;4(3):151-62.	Excluded; not relevant
16	Omar H, Shen G, Jones AS, Zoellner H, Petocz P, Darendeliler MA. Effect of low magnitude and high frequency mechanical stimuli on defects healing in cranial bones. J Oral Maxillofac Surg. 2008;66(6):1104-11.	Excluded; not relevant
17	Qamruddin I, Alam MK, Khamis MF, Husein A. Minimally Invasive Techniques to Accelerate the Orthodontic Tooth Movement: A Systematic Review of Animal Studies. Biomed Res Int. 2015;2015:608530.	Excluded; not relevant
18	Shirota T, Kamatani T, Yamaguchi T, Ogura H, Maki K, Shintani S. Effectiveness of piezoelectric surgery in reducing surgical complications after bilateral sagittal split osteotomy. Br J Oral Maxillofac Surg. 2014;52(3):219-22.	Excluded; not relevant
19	Sriram D, Jones A, Alatli-Burt I, Darendeliler MA. Effects of mechanical stimuli on adaptive remodeling of condylar cartilage. J Dent Res. 2009;88(5):466-70.	Excluded; not relevant
20	Ure DS, Oliver DR, Kim KB, Melo AC, Buschang PH. Stability changes of miniscrew implants over time. Angle Orthod. 2011;81(6):994-1000.	Excluded; not relevant
21	Vicente A, Ortiz AJ, Parra PL, Calvo JL, Chiva F. Microleakage in Class V composite and compomer restorations following exposure to a colutory prescribed for the treatment of xerostomy. Odontology. 2011;99(1):49-54.	Excluded; not relevant
22	Vieira AS, Pedro Rde L, Antunes Ldos S, Alves Dos Santos MP, Antunes LA, Primo LG, et al. Topography and presence of a smear layer in deciduous molars prepared with high-speed cutting and ultrasonic abrasion: an in-vitro study. Acta Odontol Scand. 2011;69(3):165-9.	Excluded; not relevant
23	Uribe F, Dutra E, Chandhoke T. Effect of cyclical forces on orthodontic tooth movement, from animals to humans. Orthodontics & Craniofacial Research. 2017;20:68-71.	Excluded; no clinical study
24	Elkhadem A, Sheba M. Unclear if non-surgical adjuncts accelerate orthodontic treatment. Evid Based Dent. 2017;18(1):26-7.	Excluded; no clinical study
25	Rozen D, Khoo E, El Sayed H, Niederman R, McGowan R, Alikhani M, et al. Accelerated tooth movement: Do we need a new systematic review? Seminars in Orthodontics. 2015;21(3):224-30.	Excluded; no clinical study
26	El-Angbawi A, McIntyre GT, Fleming PS, Bearn DR. Non-surgical adjunctive interventions for	Systematic

	accelerating tooth movement in patients undergoing fixed orthodontic treatment. The Cochrane database of systematic reviews. 2015;11:CD010887.	review; checked for eligible trials
27	Fleming PS, Strydom H, Katsaros C, Macdonald L, Curatolo M, Fudalej P, et al. Non-pharmacological interventions for alleviating pain during orthodontic treatment. Cochrane Database of Systematic Reviews. 2016;2016(12).	Systematic review; checked for eligible trials
28	Yi J, Xiao J, Li H, Li Y, Li X, Zhao Z. Effectiveness of adjunctive interventions for accelerating orthodontic tooth movement: a systematic review of systematic reviews. J Oral Rehabil. 2017;44(8):636-54.	Systematic review; checked for eligible trials
29	Lobre WD, Callegari BJ, Gardner G, Marsh CM, Bush AC, Dunn WJ. Pain control in orthodontics using a micropulse vibration device: A randomized clinical trial. Angle Orthodontist. 2016;86(4):625-30.	Excluded; non-eligible outcome
30	Pavlin D, Anthony R, Raj V, Gakunga PT. Cyclic loading (vibration) accelerates tooth movement in orthodontic patients: A double-blind, randomized controlled trial. Seminars in Orthodontics. 2015;21(3):187-94.	Excluded; non-eligible outcome
31	DiBiase AT, Woodhouse NR, Papageorgiou SN, Johnson N, Slipper C, Grant J, et al. Effect of supplemental vibrational force on orthodontically induced inflammatory root resorption: A multicenter randomized clinical trial. Am J Orthod Dentofacial Orthop. 2016;150(6):918-27.	Included for potential evaluation
32	Marie SS, Powers M, Sheridan JJ. Vibratory stimulation as a method of reducing pain after orthodontic appliance adjustment. J Clin Orthod. 2003;37(4):205-8; quiz 3-4.	Included for potential evaluation
33	Miles P, Fisher E. Assessment of the changes in arch perimeter and irregularity in the mandibular arch during initial alignment with the AcceleDent Aura appliance vs no appliance in adolescents: A single-blind randomized clinical trial. Am J Orthod Dentofacial Orthop. 2016;150(6):928-36.	Included for potential evaluation
34	Miles P, Smith H, Weyant R, Rinchuse DJ. The effects of a vibrational appliance on tooth movement and patient discomfort: a prospective randomised clinical trial. Aust Orthod J. 2012;28(2):213-8.	Included for potential evaluation
35	Woodhouse NR, DiBiase AT, Johnson N, Slipper C, Grant J, Alsaleh M, et al. Supplemental vibrational force during orthodontic alignment: a randomized trial. J Dent Res. 2015;94(5):682-9.	Included for potential evaluation
36	Woodhouse NR, DiBiase AT, Papageorgiou SN, Johnson N, Slipper C, Grant J, et al. Supplemental vibrational force does not reduce pain experience during initial alignment with fixed orthodontic appliances: a multicenter randomized clinical trial. Sci Rep. 2015;5:17224.	Included for potential evaluation

Supplementary Table 3c. List of included/excluded studies on the topic of piezocision.

Nr.	Paper	Status
1	Camacho AD, Velasquez Cujar SA. Dental movement acceleration: Literature review by an alternative scientific evidence method. World J Methodol. 2014;4(3):151-62.	Excluded; screening of title
2	Han KH, Park JH, Bayome M, Jeon IS, Lee W, Kook YA. Effect of Frequent Application of Low-Level Laser Therapy on Corticotomized Tooth Movement in Dogs: A Pilot Study. Journal of Oral and Maxillofacial Surgery. 2014;72(6).	Excluded; screening of title
3	Kim KA, Choi EK, Ohe JY, Ahn HW, Kim SJ. Effect of low-level laser therapy on orthodontic tooth movement into bone-grafted alveolar defects. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(4):608-17.	Excluded; screening of title
4	Kim SJ, Moon SU, Kang SG, Park YG. Effects of low-level laser therapy after Corticision on tooth movement and paradental remodeling. Lasers Surg Med. 2009;41(7):524-33.	Excluded; screening of title
5	Kim YS, Kim SJ, Yoon HJ, Lee PJ, Moon W, Park YG. Effect of piezopuncture on tooth movement and bone remodeling in dogs. Am J Orthod Dentofacial Orthop. 2013;144(1):23-31.	Excluded; screening of title
6	Koudstaal MJ, Wolvius EB, Schulten AJ, Hop WC, van der Wal KG. Stability, tipping and relapse of bone-borne versus tooth-borne surgically assisted rapid maxillary expansion; a prospective randomized patient trial. Int J Oral Maxillofac Surg. 2009;38(4):308-15.	Excluded; screening of title
7	Lee DY, Ahn HW, Herr Y, Kwon YH, Kim SH, Kim EC. Periodontal responses to augmented corticotomy with collagen membrane application during orthodontic buccal tipping in dogs. Biomed Res Int. 2014;2014:873918.	Excluded; screening of title
8	Lee KB, Lee DY, Ahn HW, Kim SH, Kim EC, Roitman I. Tooth movement out of the bony wall using augmented corticotomy with nonautogenous graft materials for bone regeneration. Biomed Res Int. 2014;2014:347508.	Excluded; screening of title
9	Ma Z, Xu G, Yang C, Xie Q, Shen Y, Zhang S. Efficacy of the technique of piezoelectric corticotomy for orthodontic traction of impacted mandibular third molars. Br J Oral Maxillofac Surg. 2015;53(4):326-31.	Excluded; screening of title
10	Mertens B, Angioni C, Orti V, Canal P. [Collaboration between periodontics and orthodontics: interest of alveolar corticotomies and piezocision. Review of literature]. Orthod Fr. 2017;88(2):179-91.	Excluded; screening of title
11	Murphy CA, Chandhoke T, Kalajzic Z, Flynn R, Utreja A, Wadhwa S, et al. Effect of corticision and different force magnitudes on orthodontic tooth movement in a rat model. Am J Orthod Dentofacial Orthop. 2014;146(1):55-66.	Excluded; screening of title
12	Sanjideh PA, Rossouw PE, Campbell PM, Opperman LA, Buschang PH. Tooth movements in foxhounds after one or two alveolar corticotomies. European Journal of Orthodontics. 2010;32(1):106-13.	Excluded; screening of title
13	Vasconcelos B, Caubi A, Dias E, Lago C, Porto G. Surgically assisted rapid maxillary expasion: a preliminar study. Brazilian journal of otorhinolaryngology [Internet]. 2006; 72(4):[457-61 pp.].	Excluded; screening of title
14	Wang L, Lee W, Lei DL, Liu YP, Yamashita DD, Yen SL. Tisssue responses in corticotomy- and osteotomy-assisted tooth movements in rats: histology and immunostaining. Am J Orthod Dentofacial Orthop. 2009;136(6):770.e1-11; discussion -1.	Excluded; screening of title
15	Yu F, Feng D, Yi Z, Yaling Z, Xiangfeng Z, He Z, et al. [Three-dimensional morphological analysis of corticotomy-assisted intrusion of premolars in Beagle dogs]. Hua Xi Kou Qiang Yi Xue Za Zhi. 2016;34(3):267-71.	Excluded; screening of title
16	Zhu SY, Yuan CY, Liu ZX, Li XM, Wang PL. [The mechanism of corticotomy accelerating orthodontic tooth movement in SD rats]. Shanghai Kou Qiang Yi Xue. 2017;26(1):12-6.	Excluded; screening of title
17	Abdallah MN, Flores-Mir C. Are interventions for accelerating orthodontic tooth movement effective? Evid Based Dent. 2014;15(4):116-7.	Excluded; screening of abstract
18	Fleming PS. Accelerating orthodontic tooth movement using surgical and non-surgical approaches. Evid Based Dent. 2014;15(4):114-5.	Excluded; screening of abstract
19	Iglesias-Linares A, Yanez-Vico RM, Moreno-Fernandez AM, Mendoza-Mendoza A, Solano-Reina E. Corticotomy-assisted orthodontic enhancement by bone morphogenetic protein-2 administration. J Oral Maxillofac Surg. 2012;70(2):e124-32.	Excluded; screening of abstract
20	Lee W, Karapetyan G, Moats R, Yamashita DD, Moon HB, Ferguson DJ, et al. Corticotomy-/osteotomy-assisted tooth movement microCTs differ. J Dent Res. 2008;87(9):861-7.	Excluded; screening of abstract
21	Shoreibah EA, Ibrahim SA, Attia MS, Diab MM. Clinical and radiographic evaluation of bone grafting in corticotomy-facilitated orthodontics in adults. J Int Acad Periodontol. 2012;14(4):105-13.	Excluded; missing fulltext
22	Shoreibah EA, Salama AE, Attia MS, Abu-Seida SM. Corticotomy-facilitated orthodontics in adults using a further modified technique. J Int Acad Periodontol. 2012;14(4):97-104.	Excluded; missing fulltext
23	Qamruddin I, Alam MK, Khamis MF, Husein A. Minimally Invasive Techniques to Accelerate the Orthodontic Tooth Movement: A Systematic Review of Animal Studies. Biomed Res Int. 2015;2015:608530.	Excluded; not relevant
24	Nimeri G, Kau CH, Abou-Kheir NS, Corona R. Acceleration of tooth movement during orthodontic treatment - a frontier in Orthodontics. Progress in Orthodontics. 2013;14(1):1-8.	Excluded; no clinical study
25	Rozen D, Khoo E, El Sayed H, Niederman R, McGowan R, Alikhani M, et al. Accelerated tooth movement: Do we need a new systematic review? Seminars in Orthodontics. 2015;21(3):224-30.	Excluded; no clinical study
26	Alwafi A. Inconclusive evidence for the effectiveness of nonconventional methods in accelerating orthodontic tooth movement. Journal of the American Dental Association. 2017;148(3):193-4.	Excluded; no clinical study
27	Koudstaal MJ, Poort LJ, van der Wal KGH, Wolvius EB, Prahl-Andersen B, Schulten AJM.	Excluded; no

	Surgically assisted rapid maxillary expansion (SARME): a review of the literature. Int J Oral Maxillofac Surg. 2005;34(7):709-14.	clinical study
28	Alfawal AM, Hajeer MY, Ajaj MA, Hamadah O, Brad B. Effectiveness of minimally invasive surgical procedures in the acceleration of tooth movement: a systematic review and meta-analysis. Prog Orthod. 2016;17(1):33.	Systematic review; checked for eligible trials
29	Gkantidis N, Mistakidis I, Kouskoura T, Pandis N. Effectiveness of non-conventional methods for accelerated orthodontic tooth movement: A systematic review and meta-analysis. Journal of Dentistry. 2014;42(10):1300-19.	Systematic review; checked for eligible trials
30	Hassan AH, Al-Saeed SH, Al-Maghlouth BA, Bahammam MA, Linjawi AI, El-Bialy TH. Corticotomy-assisted orthodontic treatment. A systematic review of the biological basis and clinical effectiveness. Saudi Med J. 2015;36(7):794-801.	Systematic review; checked for eligible trials
31	Hoogeveen EJ, Jansma J, Ren Y. Surgically facilitated orthodontic treatment: a systematic review. Am J Orthod Dentofacial Orthop. 2014;145(4 Suppl):S51-64.	Systematic review; checked for eligible trials
32	Kalemaj Z, Debernard IC, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: a systematic review. Eur J Oral Implantol. 2015;8(1):9-24.	Systematic review; checked for eligible trials
33	Long H, Pyakurel U, Wang Y, Liao L, Zhou Y, Lai W. Interventions for accelerating orthodontic tooth movement: A systematic review. Angle Orthodontist. 2013;83(1):164-71.	Systematic review; checked for eligible trials
34	Patterson BM, Dalci O, Darendeliler MA, Papadopoulou AK. Corticotomies and Orthodontic Tooth Movement: A Systematic Review. J Oral Maxillofac Surg. 2016;74(3):453-73.	Systematic review; checked for eligible trials
35	Yi J, Xiao J, Li Y, Li X, Zhao Z. Efficacy of piezocision on accelerating orthodontic tooth movement: A systematic review. Angle Orthod. 2017;87(4):491-8.	Systematic review; checked for eligible trials
36	Fernandez-Ferrer L, Montiel-Company JM, Candel-Marti E, Almerich-Silla JM, Penarrocha-Diago M, Bellot-Arcis C. Corticotomies as a surgical procedure to accelerate tooth movement during orthodontic treatment: A systematic review. Med Oral Patol Oral Cir Bucal. 2016;21(6):e703-e12.	Systematic review; checked for eligible trials
37	Yi J, Xiao J, Li H, Li Y, Li X, Zhao Z. Effectiveness of adjunctive interventions for accelerating orthodontic tooth movement: a systematic review of systematic reviews. J Oral Rehabil. 2017;44(8):636-54.	Systematic review; checked for eligible trials
38	Hoffmann S, Papadopoulos N, Visel D, Visel T, Jost-Brinkmann PG, Prager TM. Influence of piezotomy and osteoperforation of the alveolar process on the rate of orthodontic tooth movement: a systematic review. J Orofac Orthop. 2017;78(4):301-11.	Systematic review; checked for eligible trials
39	Liem AM, Hoogeveen EJ, Jansma J, Ren Y. Surgically facilitated experimental movement of teeth: systematic review. Br J Oral Maxillofac Surg. 2015;53(6):491-506.	Systematic review; checked for eligible trials
40	Swapp A, Campbell PM, Spears R, Buschang PH. Flapless cortical bone damage has no effect on medullary bone mesial to teeth being moved. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;147(5):547-58.	Excluded; animal study
41	Lee JK, Chung KR, Baek SH. Treatment outcomes of orthodontic treatment, corticotomy-assisted orthodontic treatment, and anterior segmental osteotomy for bimaxillary dentoalveolar protrusion. Plast Reconstr Surg. 2007;120(4):1027-36.	Excluded; no randomisation
42	Bahammam MA. Effectiveness of bovine-derived xenograft versus bioactive glass with periodontally accelerated osteogenic orthodontics in adults: a randomized, controlled clinical trial. Bmc Oral Health. 2016;16.	Excluded; different intervention to the registered trial
43	Abbas NH, Sabet NE, Hassan IT. Evaluation of corticotomy-facilitated orthodontics and piezocision in rapid canine retraction. Am J Orthod Dentofacial Orthop. 2016;149(4):473-80.	Excluded; non-eligible outcome
44	Aboul-Ela S, El-Beialy AR, El-Sayed KMF, Selim EMN, El-Mangoury NH, Mostafa YA. Miniscrew implant-supported maxillary canine retraction with and without corticotomy-facilitated orthodontics. American Journal of Orthodontics and Dentofacial Orthopedics. 2011;139(2):252-9.	Excluded; non-eligible outcome
45	Al-Naoum F, Hajeer MY, Al-Jundi A. Does alveolar corticotomy accelerate orthodontic tooth movement when retracting upper canines? A split-mouth design randomized controlled trial. J Oral Maxillofac Surg. 2014;72(10):1880-9.	Excluded; non-eligible outcome
46	Bhattacharya P, Bhattacharya H, Anjum A, Bhandari R, Agarwal DK, Gupta A, et al. Assessment of Corticotomy Facilitated Tooth Movement and Changes in Alveolar Bone Thickness - A CT Scan Study. J Clin Diagn Res. 2014;8(10):Zc26-30.	Excluded; non-eligible outcome
47	Cassetta M, Di Carlo S, Giansanti M, Pompa V, Pompa G, Barbato E. The impact of osteotomy technique for corticotomy-assisted orthodontic treatment (CAOT) on oral health-related quality of life. Eur Rev Med Pharmacol Sci. 2012;16(12):1735-40.	Excluded; non-eligible outcome
48	Jahanbakhshi MR, Motamedi AM, Feizbakhsh M, Mogharehabed A. The effect of buccal corticotomy on accelerating orthodontic tooth movement of maxillary canine. Dent Res J (Isfahan). 2016;13(4):303-8.	Excluded; non-eligible outcome
49	Charavet C, Lecloux G, Bruwier A, Rompen E, Maes N, Limme M, et al. Localized Piezoelectric Alveolar Decortication for Orthodontic Treatment in Adults: A Randomized Controlled Trial. J Dent Res. 2016;95(9):1003-9.	Included for potential evaluation; no full data available
50	Uribe F, Davoody L, Mehr R, Jayaratne YS, Almas K, Sobue T, et al. Efficiency of piezotome-corticision assisted orthodontics in alleviating mandibular anterior crowding-a randomized clinical trial. Eur J Orthod. 2017.	Included for potential evaluation

Supplementary Table 3d. List of included/excluded studies on the topic of maxillary protraction for maxillary deficiency.

Nr.	Paper	Status
1	Chung EH, Borzabadi-Farahani A, Yen SL. Clinicians and laypeople assessment of facial attractiveness in patients with cleft lip and palate treated with LeFort I surgery or late maxillary protraction. Int J Pediatr Otorhinolaryngol. 2013;77(9):1446-50.	Excluded; screening of title
2	Shadrick V, Walker M. Facemask therapy between ages six to ten years may lead to short term improvements for Class III malocclusions. Evid Based Dent. 2013;14(4):112-3.	Excluded; screening of title
3	Long H, Jian F, Lai W. Weak evidence supports the short-term benefits of orthopaedic treatment for Class III malocclusion in children. Evid Based Dent. 2014;15(1):21-2.	Excluded; screening of title
4	Stamm T, Meier N, Hohoff A, Meyer U, Heinecke A, Joos U. Are collimated low-dose digital radiographs valid for performing Delaire's architectural analysis? International Journal of Oral and Maxillofacial Surgery. 2003;32(6):600-5.	Excluded; screening of title
5	Ghafari JG, Haddad RV, Saadeh ME. Class III Malocclusion-The Evidence on Diagnosis and Treatment. Evidence-Based Orthodontics. 2011:247-80.	Excluded; screening of title
6	Zimmer B, Schenk-Kazan S. Dental compensation for skeletal Class III malocclusion by isolated extraction of mandibular teeth. Part 1: Occlusal situation 12 years after completion of active treatment. Journal of Orofacial Orthopedics-Fortschritte Der Kieferorthopadie. 2015;76(3):251-64.	Excluded; screening of title
7	Staudt CB, Kiliaridis S. Different skeletal types underlying Class III malocclusion in a random population. American Journal of Orthodontics and Dentofacial Orthopedics. 2009;136(5):715-21.	Excluded; screening of title
8	Freire AB, do Nascimento LEAG, de Lira ALS. Effects induced after the use of maxillary protraction appliances: A literature review. Dental Press Journal of Orthodontics. 2012;17(4):122-8.	Excluded; screening of title
9	Kalha AS. Face mask protraction therapy in early skeletal class III malocclusion: Does rapid palatal expansion enhance the efficiency of maxillary protraction with a face mask in developing class III malocclusions? Evidence-Based Dentistry. 2006;7(1):16-7.	Excluded; screening of title
10	Seehra J, Fleming PS, Mandall N, Dibiase AT. A comparison of two different techniques for early correction of Class III malocclusion. Angle Orthod. 2012;82(1):96-101.	Excluded; screening of abstract
11	Solano-Mendoza B, Iglesias-Linares A, Yanez-Vico RM, Mendoza-Mendoza A, Alio-Sanz JJ, Solano-Reina E. Maxillary protraction at early ages. The revolution of new bone anchorage appliances. J Clin Pediatr Dent. 2012;37(2):219-29.	Excluded; screening of abstract
12	De Clerck HJ, Proffit WR. Growth modification of the face: A current perspective with emphasis on Class III treatment. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(1):37-46.	Excluded; screening of abstract
13	Yepes E, Quintero P, Rueda ZV, Pedroza A. Optimal force for maxillary protraction facemask therapy in the early treatment of class III malocclusion. Eur J Orthod. 2014;36(5):586-94.	Excluded; screening of abstract
14	Moon H, Turley P. Maxillary protraction therapy on Class III malocclusion: randomized clinical trial. IADR General Session; 2010, Jul 14-17; Barcelona, Spain [Internet]. 2010:[3553.	Excluded; missing fulltext
15	Poletti L, Scaglione F, Tripodi SM, Esposito L, Farronato G. Orthopedic treatment for class III malocclusion: A systematic review. Mondo Ortodontico. 2012;37(3):96-106.	Excluded; missing fulltext
16	Ge YS, Liu J, Chen L, Han JL, Guo X. Dentofacial effects of two facemask therapies for maxillary protraction Miniscrew implants versus rapid maxillary expanders. Angle Orthodontist. 2012;82(6):1083-91.	Excluded; not relevant
17	Jamilian A, Cannavale R, Piancino MG, Eslami S, Perillo L. Methodological quality and outcome of systematic reviews reporting on orthopaedic treatment for class III malocclusion: Overview of systematic reviews. J Orthod. 2016;43(2):102-20.	Excluded; not relevant
18	Perrone APR, Mucha JN. The treatment of Class III- Systematic review - Part I. Magnitude, direction and duration of the forces in the maxillary protraction. Revista Dental Press de Ortodontia e Ortopedia Facial. 2009;14(5):109-17.	Excluded; not relevant
19	Turley PK. Managing the developing Class III malocclusion with palatal expansion and facemask therapy. American Journal of Orthodontics and Dentofacial Orthopedics. 2002;122(4):349-52.	Excluded; no clinical study
20	Woon SC, Thiruvenkatachari B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017;151(1):28-52.	Systematic review; checked for eligible trials
21	Foersch M, Jacobs C, Wriedt S, Hechtner M, Wehrbein H. Effectiveness of maxillary protraction using facemask with or without maxillary expansion: a systematic review and meta-analysis. Clin Oral Investig. 2015;19(6):1181-92.	Systematic review; checked for eligible trials
22	Cordasco G, Matarese G, Rustico L, Fastuca S, Caprioglio A, Lindauer SJ, et al. Efficacy of orthopedic treatment with protraction facemask on skeletal Class III malocclusion: a systematic review and meta-analysis. Orthod Craniofac Res. 2014;17(3):133-43.	Systematic review; checked for eligible trials
23	Watkinson S, Harrison JE, Furness S, Worthington HV. Orthodontic treatment for prominent lower front teeth (Class III malocclusion) in children. Cochrane Database Syst Rev. 2013(9):Cd003451.	Systematic review; checked for eligible trials
24	Morales-Fernandez M, Iglesias-Linares A, Yanez-Vico RM, Mendoza-Mendoza A, Solano-Reina E. Bone- and dentoalveolar-anchored dentofacial orthopedics for Class III malocclusion: new approaches, similar objectives? : a systematic review. Angle Orthod. 2013;83(3):540-52.	Systematic review; checked for eligible trials
25	Kim JH, Viana MA, Graber TM, Omerza FF, BeGole EA. The effectiveness of protraction face mask therapy: a meta-analysis. Am J Orthod Dentofacial Orthop. 1999;115(6):675-85.	Systematic review; checked for eligible trials
26	Feng XX, Li JH, Li Y, Zhao ZH, Zhao S, Wang J. Effectiveness of TAD-anchored maxillary protraction in late mixed dentition A systematic review. Angle Orthodontist. 2012;82(6):1107-14.	Systematic review; checked for eligible

		trials
27	Zhang W, Qu HC, Yu M, Zhang Y. The Effects of Maxillary Protraction with or without Rapid Maxillary Expansion and Age Factors in Treating Class III Malocclusion: A Meta-Analysis. PLoS One. 2015;10(6):e0130096.	Systematic review; checked for eligible trials
28	Pithon MM, Santos NL, Santos CR, Baiao FC, Pinheiro MC, Matos MN, et al. Is alternate rapid maxillary expansion and constriction an effective protocol in the treatment of Class III malocclusion? A systematic review. Dental Press J Orthod. 2016;21(6):34-42.	Systematic review; checked for eligible trials
29	Major MP, Wong JK, Saltaji H, Major PW, Flores-Mir C. Skeletal anchored maxillary protraction for midface deficiency in children and early adolescents with Class III malocclusion: A systematic review and meta-analysis. Journal of the World Federation of Orthodontists. 2012;1(2):e47-e54.	Systematic review; checked for eligible trials
30	Rongo R, D'Anto V, Bucci R, Polito I, Martina R, Michelotti A. Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. J Oral Rehabil. 2017;44(7):545-62.	Systematic review; checked for eligible trials
31	Jager A, Braumann B, Kim C, Wahner S. Skeletal and dental effects of maxillary protraction in patients with angle class III malocclusion. A meta-analysis. J Orofac Orthop. 2001;62(4):275-84.	Systematic review; checked for eligible trials
32	Akin M, Ucar FI, Chousein C, Sari Z. Effects of chincup or facemask therapies on the orofacial airway and hyoid position in Class III subjects. J Orofac Orthop. 2015;76(6):520-30.	Excluded; no randomisation
33	Arman A, Ufuk Toygar T, Abuhijleh E. Evaluation of maxillary protraction and fixed appliance therapy in Class III patients. Eur J Orthod. 2006;28(4):383-92.	Excluded; no randomisation
34	Martin O, Muelas L, Vinas MJ. Comparative study of nasopharyngeal soft-tissue characteristics in patients with Class III malocclusion. American Journal of Orthodontics and Dentofacial Orthopedics. 2011;139(2):242-51.	Excluded; no randomisation
35	Canturk BH, Celikoglu M. Comparison of the effects of face mask treatment started simultaneously and after the completion of the alternate rapid maxillary expansion and constriction procedure. Angle Orthod. 2015;85(2):284-91.	Excluded; different intervention to the registered trial
36	Celikoglu M, Yavuz I, Unal T, Oktay H, Erdem A. Comparison of the soft and hard tissue effects of two different protraction mechanisms in class III patients: a randomized clinical trial. Clin Oral Investig. 2015;19(8):2115-22.	Excluded; different intervention to the registered trial
37	Liu W, Song Y, Wang X, He D, Zhou Y. [A cone-beam computed tomography evaluation of maxillary protraction with repetitive rapid palatal expansions and constrictions]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2015;50(2):78-83.	Excluded; different intervention to the registered trial
38	Elnagar MH, Elshourbagy E, Ghobashy S, Khedr M, Evans CA. Dentoalveolar and arch dimension changes in patients treated with miniplate-anchored maxillary protraction. Am J Orthod Dentofacial Orthop. 2017;151(6):1092-106.	Excluded; different intervention to the registered trial
39	Ge YS, Liu J, Chen L, Han JL, Guo X. Dentofacial effects of two facemask therapies for maxillary protraction. Angle Orthod. 2012;82(6):1083-91.	Excluded; different intervention to the registered trial
40	Husson AH, Burhan AS, Salma FB, Nawaya FR. Dentoskeletal Effects of the Modified Tandem Appliance vs the Facemask Appliance in the Treatment of Skeletal Class III Malocclusion: A Single-center, Randomized Controlled Trial. J Contemp Dent Pract. 2016;17(7):522-9.	Excluded; different intervention to the registered trial
41	Liu W, Zhou Y, Wang X, Liu D, Zhou S. Effect of maxillary protraction with alternating rapid palatal expansion and constriction vs expansion alone in maxillary retrusive patients: a single-center, randomized controlled trial. Am J Orthod Dentofacial Orthop. 2015;148(4):641-51.	Excluded; different intervention to the registered trial
42	Liu WT, Zhou YH. [Effect of repetitive rapid palatal expansions and constrictions by double hinged expander in maxillary protraction cases]. Beijing Da Xue Xue Bao. 2013;45(1):69-76.	Excluded; different intervention to the registered trial
43	Chen XH, Xie XQ. [The effect of two different methods of rapid maxillary expansion on treatment results of skeletal Class III malocclusion patients with maxillary protraction in early permanent dentition]. Shanghai Kou Qiang Yi Xue. 2012;21(5):580-3.	Excluded; different intervention to the registered trial
44	Keles A, Tokmak EC, Erverdi N, Nanda R. Effect of varying the force direction on maxillary orthopedic protraction. Angle Orthod. 2002;72(5):387-96.	Excluded; different intervention to the registered trial
45	Showkatbakhsh R, Jamilian A, Taban T, Golrokh M. The effects of face mask and tongue appliance on maxillary deficiency in growing patients: a randomized clinical trial. Prog Orthod. 2012;13(3):266-72.	Excluded; different intervention to the registered trial
46	Showkatbakhsh R, Toumarian L, Jamilian A, Sheibaninia A, Mirkarimi M, Taban T. The effects of face mask and tongue plate on maxillary deficiency in growing patients: a randomized clinical trial. J Orthod. 2013;40(2):130-6.	Excluded; different intervention to the registered trial
47	Jamilian A, Haraji A, Showkatbakhsh R, Valaee N. The effects of miniscrew with Class III traction in growing patients with maxillary deficiency. Int J Orthod Milwaukee. 2011;22(2):25-30.	Excluded; different intervention to the registered trial
48	Kurt H, Alioglu C, Karayazgan B, Tuncer N, Kilicoglu H. The effects of two methods of Class III malocclusion treatment on temporomandibular disorders. Eur J Orthod. 2011;33(6):636-41.	Excluded; different intervention to the registered trial
49	Zhang H, Liu J, Fan XF, Zhao Q, Zhang JH, Zhao ZH. [Modified retention elements of removable reverse headgear appliances]. Hua Xi Kou Qiang Yi Xue Za Zhi. 2008;26(3):306-7, 11.	Excluded; different intervention to the registered trial
50	Saleh M, Hajeer MY, Al-Jundi A. Short-term soft- and hard-tissue changes following Class III treatment using a removable mandibular retractor: a randomized controlled trial. Orthodontics & Craniofacial Research. 2013;16(2):75-86.	Excluded; different intervention to the registered trial
51	Showkatbakhsh R, Jamilian A, Ghassemi M, Ghassemi A, Taban T, Imani Z. Theeffectsoffacemaskandreversechin cup on maxillary deficient patients. J Orthod.	Excluded; different intervention to the

	2012;39(2):95-101.	registered trial
52	Anne Mandall N, Cousley R, DiBiase A, Dyer F, Littlewood S, Mattick R, et al. Is early Class III protraction facemask treatment effective? A multicentre, randomized, controlled trial: 3-year follow-up. J Orthod. 2012;39(3):176-85.	Included for potential evaluation
53	Mandall N, Cousley R, DiBiase A, Dyer F, Littlewood S, Mattick R, et al. Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. J Orthod. 2016;43(3):164-75.	Included for potential evaluation
54	Mandall N, DiBiase A, Littlewood S, Nute S, Stivaros N, McDowall R, et al. Is early Class III protraction facemask treatment effective? A multicentre, randomized, controlled trial: 15-month follow-up. J Orthod. 2010;37(3):149-61.	Included for potential evaluation
55	Vaughn GA, Mason B, Moon HB, Turley PK. The effects of maxillary protraction therapy with or without rapid palatal expansion: a prospective, randomized clinical trial. Am J Orthod Dentofacial Orthop. 2005;128(3):299-309.	Included for potential evaluation
56	Xu B, Lin J. The orthopedic treatment of skeletal class III malocclusion with maxillary protraction therapy. Chin J Stomatol 2001;36:401-3.	Included for potential evaluation

Supplementary Table 3e. List of included/excluded studies on the topic of skeletal anchorage for space closure.

Nr.	Paper	Status
1	Reynders R, Ronchi L, Bipat S. Mini-implants in orthodontics: a systematic review of the literature. Am J Orthod Dentofacial Orthop. 2009;135(5):564 e1-19; discussion -5.	Excluded; screening of abstract
2	Favero L, Pisani C, Stellini E. A comparative analysis of TADs with reference to their use in the treatment of Class II malocclusion. Mondo Ortodontico. 2008;33(6):361-402.	Excluded; missing fulltext
3	Maddalone M, Ferrari M, Stanizzi A, Barrilà S, Arrigoni P. Use of miniscrew implants in orthodontic distal movement. Dental Cadmos. 2010;78(8):97-105.	Excluded; missing fulltext
4	Al-Kalaly AA, Wong RWK, Cheung LK, Purkayastha SK, Schatzle M, Rabie ABM. Evaluation of bone thickness around the mental foramen for potential fixation of a bone-borne functional appliance: a computer tomography scan study. Clin Oral Implants Res. 2010;21(11):1288-93.	Excluded; not relevant
5	Alsafadi AS, Alabdullah MM, Saltaji H, Abdo A, Youssef M. Effect of molar intrusion with temporary anchorage devices in patients with anterior open bite: a systematic review. Prog Orthod. 2016;17:9.	Excluded; not relevant
6	AlSamak S, Gkantidis N, Bitsanis E, Christou P. Assessment of potential orthodontic mini-implant insertion sites based on anatomical hard tissue parameters: a systematic review. Int J Oral Maxillofac Implants. 2012;27(4):875-87.	Excluded; not relevant
7	Alsamak S, Psomiadis S, Gkantidis N. Positional guidelines for orthodontic mini-implant placement in the anterior alveolar region: a systematic review. Int J Oral Maxillofac Implants. 2013;28(2):470-9.	Excluded; not relevant
8	Al-Suleiman M, Shehadah M. AUSOM: a 3D placement guide for orthodontic mini-implants. Orthodontics (Chic). 2011;12(1):28-37.	Excluded; not relevant
9	Alves M, Jr., Baratieri C, Mattos CT, Araujo MT, Maia LC. Root repair after contact with mini-implants: systematic review of the literature. Eur J Orthod. 2013;35(4):491-9.	Excluded; not relevant
10	Aras I, Tuncer AV. Comparison of anterior and posterior mini-implant-assisted maxillary incisor intrusion: Root resorption and treatment efficiency. Angle Orthod. 2016;86(5):746-52.	Excluded; not relevant
11	Aslan BI, Kucukkaraca E, Turkoz C, Dincer M. Treatment effects of the Forsus Fatigue Resistant Device used with miniscrew anchorage. Angle Orthod. 2014;84(1):76-87.	Excluded; not relevant
12	Baxmann M, McDonald F, Bourauel C, Jager A. Expectations, acceptance, and preferences regarding microimplant treatment in orthodontic patients: A randomized controlled trial. American Journal of Orthodontics and Dentofacial Orthopedics. 2010;138(3).	Excluded; not relevant
13	Bidra AS, Almas K. Mini implants for definitive prosthodontic treatment: a systematic review. J Prosthet Dent. 2013;109(3):156-64.	Excluded; not relevant
14	Borsos G, Jianu R, Vegh A. Comparison of bone-borne and tooth tissue-borne anchorage during the maxillary canine retraction in growing patients: A randomised clinical trial. Timisoara Medical Journal. 2011;61(1-2):98-101.	Excluded; not relevant
15	Brisceno CE, Rossouw PE, Carrillo R, Spears R, Buschang PH. Healing of the roots and surrounding structures after intentional damage with miniscrew implants. Am J Orthod Dentofacial Orthop. 2009;135(3):292-301.	Excluded; not relevant
16	Bueno Medeiros R, Cardoso de Araújo LF, Mucha JN, Trindade Motta A. Stability of open-bite treatment in adult patients: A systematic review. Journal of the World Federation of Orthodontists. 2012;1(3):e97-e101.	Excluded; not relevant
17	Carney LO, Campbell PM, Spears R, Ceen RF, Melo AC, Buschang PH. Effects of pilot holes on longitudinal miniscrew stability and bony adaptation. Am J Orthod Dentofacial Orthop. 2014;146(5):554-64.	Excluded; not relevant
18	Carrillo R, Buschang PH, Opperman LA, Franco PF, Rossouw PE. Segmental intrusion with mini-screw implant anchorage: a radiographic evaluation. Am J Orthod Dentofacial Orthop. 2007;132(5):576 e1-6.	Excluded; not relevant
19	Carrillo R, Rossouw PE, Franco PF, Opperman LA, Buschang PH. Intrusion of multiradicular teeth and related root resorption with mini-screw implant anchorage: a radiographic evaluation. Am J Orthod Dentofacial Orthop. 2007;132(5):647-55.	Excluded; not relevant
20	Celebi AA, Demirer S, Catalbas B, Arikan S. Effect of ovarian activity on orthodontic tooth movement and gingival crevicular fluid levels of interleukin-1beta and prostaglandin E(2) in cats. Angle Orthod. 2013;83(1):70-5.	Excluded; not relevant
21	Changsiripun C, Phusantisampan P. Attitudes of orthodontists and laypersons towards tooth extractions and additional anchorage devices. Prog Orthod. 2017;18(1):19.	Excluded; not relevant
22	Chatzigianni A, Keilig L, Duschner H, Gotz H, Eliades T, Bourauel C. Comparative analysis of numerical and experimental data of orthodontic mini-implants. Eur J Orthod. 2011;33(5):468-75.	Excluded; not relevant
23	Chen Y, Kyung HM, Zhao WT, Yu WJ. Critical factors for the success of orthodontic mini-implants: A systematic review. American Journal of Orthodontics and Dentofacial Orthopedics. 2009;135(3):284-91.	Excluded; not relevant
24	Chen YH, Chang HH, Chen YJ, Lee D, Chiang HH, Yao CC. Root contact during insertion of miniscrews for orthodontic anchorage increases the failure rate: an animal study. Clin Oral Implants Res. 2008;19(1):99-106.	Excluded; not relevant
25	Chhibber A, Upadhyay M. En-masse protraction of mandibular posterior teeth into missing mandibular lateral incisor spaces using a fixed functional appliance. American Journal of Orthodontics and Dentofacial Orthopedics. 2016;150(5):864-75.	Excluded; not relevant

26	Choi SH, Jang SH, Cha JYP, Hwang CJ. Evaluation of the surface characteristics of anodic oxidized miniscrews and their impact on biomechanical stability: An experimental study in beagle dogs. American Journal of Orthodontics and Dentofacial Orthopedics. 2016;149(1):31-8.	Excluded; not relevant
27	Choi YJ, Kim KH, Lee KJ, Chung CJ, Park YC. Histomorphometric evaluation of maxillary molar roots and surrounding periodontium following molar intrusion in rats. Orthod Craniofac Res. 2015;18(1):12-20.	Excluded; not relevant
28	Cohen G, Campbell PM, Rossouw PE, Buschang PH. Effects of increased surgical trauma on rates of tooth movement and apical root resorption in foxhound dogs. Orthod Craniofac Res. 2010;13(3):179-90.	Excluded; not relevant
29	Cuairan C, Campbell PM, Kontogiorgos E, Taylor RW, Melo AC, Buschang PH. Local application of zoledronate enhances miniscrew implant stability in dogs. Am J Orthod Dentofacial Orthop. 2014;145(6):737-49.	Excluded; not relevant
30	Da Silva VC, Cirelli CC, Ribeiro FS, Leite FRM, Benatti Neto C, Marcantonio RAC, et al. Intrusion of teeth with class III furcation: A clinical, histologic and histometric study in dogs. Journal of Clinical Periodontology. 2008;35(9):807-16.	Excluded; not relevant
31	Dalessandri D, Salgarello S, Dalessandri M, Lazzaroni E, Piancino M, Paganelli C, et al. Determinants for success rates of temporary anchorage devices in orthodontics: a meta-analysis (n > 50). Eur J Orthod. 2014;36(3):303-13.	Excluded; not relevant
32	De Clerck HJ, Proffit WR. Growth modification of the face: A current perspective with emphasis on Class III treatment. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(1):37-46.	Excluded; not relevant
33	de Morais LS, Serra GG, Albuquerque Palermo EF, Andrade LR, Müller CA, Meyers MA, et al. Systemic levels of metallic ions released from orthodontic mini-implants. American Journal of Orthodontics and Dentofacial Orthopedics. 2009;135(4):522-9.	Excluded; not relevant
34	Dobranszki A, Faber J, Scatolino IMC, Dobranszki NPAC, de Toledo OA. Analysis of factors associated with orthodontic microscrew failure. Brazilian Dental Journal. 2014;25(4):346-51.	Excluded; not relevant
35	Ekizer A, Turker G, Uysal T, Guray E, Tasdemir Z. Light emitting diode mediated photobiomodulation therapy improves orthodontic tooth movement and miniscrew stability: A randomized controlled clinical trial. Lasers Surg Med. 2016;48(10):936-43.	Excluded; not relevant
36	Eliades T, Zinelis S, Papadopoulos MA, Eliades G. Characterization of retrieved orthodontic miniscrew implants. Am J Orthod Dentofacial Orthop. 2009;135(1):10 e1-7; discussion -1.	Excluded; not relevant
37	Elkordy SA, Aboelnaga AA, Fayed MM, AboulFotouh MH, Abouelezz AM. Can the use of skeletal anchors in conjunction with fixed functional appliances promote skeletal changes? A systematic review and meta-analysis. Eur J Orthod. 2016;38(5):532-45.	Excluded; not relevant
38	Elkordy SA, Abouelezz AM, Fayed MM, Attia KH, Ishaq RA, Mostafa YA. Three-dimensional effects of the mini-implant-anchored Forsus Fatigue Resistant Device: A randomized controlled trial. Angle Orthod. 2016;86(2):292-305.	Excluded; not relevant
39	Elkordy SA, Fayed MM, Abouelezz AM, Attia KH. Comparison of patient acceptance of the Forsus Fatigue Resistant Device with and without mini-implant anchorage: a randomized controlled trial. Am J Orthod Dentofacial Orthop. 2015;148(5):755-64.	Excluded; not relevant
40	Elnagar MH, Elshourbagy E, Ghobashy S, Khedr M, Evans CA. Dentoalveolar and arch dimension changes in patients treated with miniplate-anchored maxillary protraction. Am J Orthod Dentofacial Orthop. 2017;151(6):1092-106.	Excluded; not relevant
41	Enhos S, Veli I, Cakmak O, Ucar FI, Alkan A, Uysal T. OPG and RANKL levels around miniscrew implants during orthodontic tooth movement. Am J Orthod Dentofacial Orthop. 2013;144(2):203-9.	Excluded; not relevant
42	Ersahan S, Sabuncuoglu FA. Effects of magnitude of intrusive force on pulpal blood flow in maxillary molars. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(1):83-9.	Excluded; not relevant
43	Falkensammer F, Arnhart C, Krall C, Schaden W, Freudenthaler J, Bantleon HP. Impact of extracorporeal shock wave therapy (ESWT) on orthodontic tooth movement-a randomized clinical trial. Clin Oral Investig. 2014;18(9):2187-92.	Excluded; not relevant
44	Falkensammer F, Rausch-Fan X, Arnhart C, Krall C, Schaden W, Freudenthaler J. Impact of extracorporeal shock-wave therapy on the stability of temporary anchorage devices in adults: a single-center, randomized, placebo-controlled clinical trial. Am J Orthod Dentofacial Orthop. 2014;146(4):413-22.	Excluded; not relevant
45	Feng X, Li J, Li Y, Zhao Z, Zhao S, Wang J. Effectiveness of TAD-anchored maxillary protraction in late mixed dentition. Angle Orthod. 2012;82(6):1107-14.	Excluded; not relevant
46	Ge YS, Liu J, Chen L, Han JL, Guo X. Dentofacial effects of two facemask therapies for maxillary protraction. Angle Orthod. 2012;82(6):1083-91.	Excluded; not relevant
47	Ghafari JG. Centennial inventory: The changing face of orthodontics. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(5):732-9.	Excluded; not relevant
48	Gritsch K, Laroche N, Morgon L, Al-Hity R, Vico L, Colon P, et al. A systematic review of methods for tissue analysis in animal studies on orthodontic mini-implants. Orthod Craniofac Res. 2012;15(3):135-47.	Excluded; not relevant
49	Hembree M, Buschang PH, Carrillo R, Spears R, Rossouw PE. Effects of intentional damage of the roots and surrounding structures with miniscrew implants. Am J Orthod Dentofacial Orthop. 2009;135(3):280 e1-9; discussion -1.	Excluded; not relevant
50	Hong SB, Kusnoto B, Kim EJ, BeGole EA, Hwang HS, Lim HJ. Prognostic factors associated with the success rates of posterior orthodontic miniscrew implants: A	Excluded; not relevant

	subgroup meta-analysis. Korean J Orthod. 2016;46(2):111-26.	
51	Huja SS, Mason A, Fenell CE, Mo X, Hueni S, D'Atri AM, et al. Effects of short-term zoledronic acid treatment on bone remodeling and healing at surgical sites in the maxilla and mandible of aged dogs. J Oral Maxillofac Surg. 2011;69(2):418-27.	Excluded; not relevant
52	Ikeda H, Rossouw PE, Campbell PM, Kontogiorgos E, Buschang PH. Three-dimensional analysis of peri-bone-implant contact of rough-surface miniscrew implants. Am J Orthod Dentofacial Orthop. 2011;139(2):e153-63.	Excluded; not relevant
53	Iwai H, Motoyoshi M, Uchida Y, Matsuoka M, Shimizu N. Effects of tooth root contact on the stability of orthodontic anchor screws in the maxilla: Comparison between self-drilling and self-tapping methods. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;147(4):483-91.	Excluded; not relevant
54	Jamilian A, Haraji A, Showkatbakhsh R, Valaee N. The effects of miniscrew with Class III traction in growing patients with maxillary deficiency. Int J Orthod Milwaukee. 2011;22(2):25-30.	Excluded; not relevant
55	Janson G, Gigliotti MP, Estelita S, Chiqueto K. Influence of miniscrew dental root proximity on its degree of late stability. Int J Oral Maxillofac Surg. 2013;42(4):527-34.	Excluded; not relevant
56	Janssen KI, Raghoebar GM, Vissink A, Sandham A. Skeletal anchorage in orthodontics--a review of various systems in animal and human studies. Int J Oral Maxillofac Implants. 2008;23(1):75-88.	Excluded; not relevant
57	Jofre J, Cendoya P, Munoz P. Effect of Splinting Mini-Implants on Marginal Bone Loss: A Biomechanical Model and Clinical Randomized Study with Mandibular Overdentures. International Journal of Oral & Maxillofacial Implants. 2010;25(6):1137-44.	Excluded; not relevant
58	Kabalan O, Gordon J, Heo G, Lagravere MO. Nasal airway changes in bone-borne and tooth-borne rapid maxillary expansion treatments. Int Orthod. 2015;13(1):1-15.	Excluded; not relevant
59	Kalra S, Tripathi T, Rai P, Kanase A. Evaluation of orthodontic mini-implant placement: a CBCT study. Prog Orthod. 2014;15:61.	Excluded; not relevant
60	Kang HK, Chu TM, Dechow P, Stewart K, Kyung HM, Liu SS. Laser-treated stainless steel mini-screw implants: 3D surface roughness, bone-implant contact, and fracture resistance analysis. Eur J Orthod. 2016;38(2):154-62.	Excluded; not relevant
61	Kim SH, Lee SJ, Cho IS, Kim SK, Kim TW. Rotational resistance of surface-treated mini-implants. Angle Orthod. 2009;79(5):899-907.	Excluded; not relevant
62	Kumar P, Datana S, Londhe SM, Kadu A. Rate of intrusion of maxillary incisors in Class II Div 1 malocclusion using skeletal anchorage device and Connecticut intrusion arch. Med J Armed Forces India. 2017;73(1):65-73.	Excluded; not relevant
63	Lai TT, Chiou JY, Lai TC, Chen T, Chen MH. Oral health-related quality of life in orthodontic patients during initial therapy with conventional brackets or self-ligating brackets. Journal of Dental Sciences. 2017;12(2):161-72.	Excluded; not relevant
64	Landin M, Jadhav A, Yadav S, Tadinada A. A comparative study between currently used methods and Small Volume-Cone Beam Tomography for surgical placement of mini implants. Angle Orthod. 2015;85(3):446-53.	Excluded; not relevant
65	Lee JK, Chung KR, Baek SH. Treatment outcomes of orthodontic treatment, corticotomy-assisted orthodontic treatment, and anterior segmental osteotomy for bimaxillary dentoalveolar protrusion. Plast Reconstr Surg. 2007;120(4):1027-36.	Excluded; not relevant
66	Lee NK, Baek SH. Effects of the diameter and shape of orthodontic mini-implants on microdamage to the cortical bone. American Journal of Orthodontics and Dentofacial Orthopedics. 2010;138(1):8e1-8e.	Excluded; not relevant
67	Leethanakul C, Kanokkulchai S, Pongpanich S, Leepong N, Charoemratrote C. Interseptal bone reduction on the rate of maxillary canine retraction. Angle Orthod. 2014;84(5):839-45.	Excluded; not relevant
68	Liu SS, Cruz-Marroquin E, Sun J, Stewart KT, Allen MR. Orthodontic mini-implant diameter does not affect in-situ linear microcrack generation in the mandible or the maxilla. Am J Orthod Dentofacial Orthop. 2012;142(6):768-73.	Excluded; not relevant
69	Liu SS, Kyung HM, Buschang PH. Continuous forces are more effective than intermittent forces in expanding sutures. Eur J Orthod. 2010;32(4):371-80.	Excluded; not relevant
70	Liu SS, Opperman LA, Buschang PH. Effects of recombinant human bone morphogenetic protein-2 on midsagittal sutural bone formation during expansion. Am J Orthod Dentofacial Orthop. 2009;136(6):768 e1-8; discussion -9.	Excluded; not relevant
71	Liu SS, Opperman LA, Kyung HM, Buschang PH. Is there an optimal force level for sutural expansion? Am J Orthod Dentofacial Orthop. 2011;139(4):446-55.	Excluded; not relevant
72	Liu SS, Xu H, Sun J, Kontogiorgos E, Whittington PR, Misner KG, et al. Recombinant human bone morphogenetic protein-2 stimulates bone formation during interfrontal suture expansion in rabbits. Am J Orthod Dentofacial Orthop. 2013;144(2):210-7.	Excluded; not relevant
73	Livas C, Delli K, Karapsias S, Pandis N, Ren YJ. Investigation of bacteremia induced by removal of orthodontic mini-implants. Eur J Orthod. 2014;36(1):16-21.	Excluded; not relevant
74	Lu JJ, Qi T, Ge ZL. [A scanning electron microscopic study of root surface following mini-implant anchorage for maxillary incisors intrusion]. Shanghai Kou Qiang Yi Xue. 2009;18(4):406-10.	Excluded; not relevant
75	Ma D, Wang XX, Jin SM, Dong R, Liu WX, Li J, et al. [Comparison of two treatment method for maxillary incisors intrusion]. Shanghai Kou Qiang Yi Xue. 2013;22(2):206-9.	Excluded; not relevant
76	Madan MS, Liu ZJ, Gu GM, King GJ. Effects of human relaxin on orthodontic tooth movement and periodontal ligaments in rats. American Journal of Orthodontics and	Excluded; not relevant

	Dentofacial Orthopedics. 2007;131(1):8.e1-8.e10.	
77	Maddalone M, Ferrari M, Barrilà S, Arrigoni P, Stanizz A. Intrusive mechanics in orthodontics by the use of TADs. Dental Cadmos. 2010;78(7):97-106.	Excluded; not relevant
78	Major MP, Wong JK, Saltaji H, Major PW, Flores-Mir C. Skeletal anchored maxillary protraction for midface deficiency in children and early adolescents with Class III malocclusion: A systematic review and meta-analysis. Journal of the World Federation of Orthodontists. 2012;1(2):e47-e54.	Excluded; not relevant
79	Marquezan M, Mattos CT, Sant'Anna EF, de Souza MM, Maia LC. Does cortical thickness influence the primary stability of miniscrews?: A systematic review and meta-analysis. Angle Orthod. 2014;84(6):1093-103.	Excluded; not relevant
80	Massey CC, Kontogiorgos E, Taylor R, Opperman L, Dechow P, Buschang PH. Effect of force on alveolar bone surrounding miniscrew implants: a 3-dimensional microcomputed tomography study. Am J Orthod Dentofacial Orthop. 2012;142(1):32-44.	Excluded; not relevant
81	Mattos CT, Ruellas AC, Sant'Anna EF. Effect of autoclaving on the fracture torque of mini-implants used for orthodontic anchorage. J Orthod. 2011;38(1):15-20.	Excluded; not relevant
82	Melsen B, Huja SS, Chien HH, Dalstra M. Alveolar bone preservation subsequent to miniscrew implant placement in a canine model. Orthod Craniofac Res. 2015;18(2):77-85.	Excluded; not relevant
83	Meursinge Reynders R, Ronchi L, Ladu L, Di Girolamo N, de Lange J, Roberts N, et al. Barriers and facilitators to the implementation of orthodontic mini implants in clinical practice: a systematic review. Syst Rev. 2016;5(1):163.	Excluded; not relevant
84	Meursinge Reynders R, Ronchi L, Ladu L, Van Etten-Jamaludin F, Bipat S. Insertion torque and orthodontic mini-implants: a systematic review of the artificial bone literature. Proc Inst Mech Eng H. 2013;227(11):1181-202.	Excluded; not relevant
85	Migliorati M, Drago S, Gallo F, Amorfini L, Dalessandri D, Calzolari C, et al. Immediate versus delayed loading: comparison of primary stability loss after miniscrew placement in orthodontic patients-a single-centre blinded randomized clinical trial. Eur J Orthod. 2016;38(6):652-9.	Excluded; not relevant
86	Mo SS, Kim SH, Kook YA, Jeong DM, Chung KR, Nelson G. Resistance To immediate orthodontic loading of surface-treated mini-implants. Angle Orthodontist. 2010;80(1):123-9.	Excluded; not relevant
87	Morarend C, Qian F, Marshall SD, Southard KA, Grosland NM, Morgan TA, et al. Effect of screw diameter on orthodontic skeletal anchorage. Am J Orthod Dentofacial Orthop. 2009;136(2):224-9.	Excluded; not relevant
88	Mortensen MG, Buschang PH, Oliver DR, Kyung HM, Behrents RG. Stability of immediately loaded 3- and 6-mm miniscrew implants in beagle dogs--a pilot study. Am J Orthod Dentofacial Orthop. 2009;136(2):251-9.	Excluded; not relevant
89	Nienkemper M, Handschel J, Drescher D. Systematic review of mini-implant displacement under orthodontic loading. Int J Oral Sci. 2014;6(1):1-6.	Excluded; not relevant
90	Noorollahian S, Alavi S, Rafiei E. The effect of multiple processing and re-use on orthodontic mini-screw torque values. Dent Res J (Isfahan). 2015;12(3):243-7.	Excluded; not relevant
91	Owens SE, Buschang PH, Cope JB, Franco PF, Rossouw PE. Experimental evaluation of tooth movement in the beagle dog with the mini-screw implant for orthodontic anchorage. Am J Orthod Dentofacial Orthop. 2007;132(5):639-46.	Excluded; not relevant
92	Oz AA, Arici N, Arici S. The clinical and laboratory effects of bracket type during canine distalization with sliding mechanics. Angle Orthod. 2012;82(2):326-32.	Excluded; not relevant
93	Papageorgiou SN, Papadopoulos MA, Athanasiou AE. Assessing small study effects and publication bias in orthodontic meta-analyses: a meta-epidemiological study. Clin Oral Investig. 2014;18(4):1031-44.	Excluded; not relevant
94	Papageorgiou SN, Zogakis IP, Papadopoulos MA. Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. Am J Orthod Dentofacial Orthop. 2012;142(5):577-95 e7.	Excluded; not relevant
95	Parmar R, Reddy V, Reddy SK, Reddy D. Determination of soft tissue thickness at orthodontic miniscrew placement sites using ultrasonography for customizing screw selection. Am J Orthod Dentofacial Orthop. 2016;150(4):651-8.	Excluded; not relevant
96	Pulver RJ, Campbell PM, Opperman LA, Buschang PH. Miniscrew-assisted slow expansion of mature rabbit sutures. Am J Orthod Dentofacial Orthop. 2016;150(2):303-12.	Excluded; not relevant
97	Raji SH, Noorollahian S, Niknam SM. The effect of insertion angle on orthodontic mini-screw torque. Dent Res J (Isfahan). 2014;11(4):448-51.	Excluded; not relevant
98	Ramirez-Echave JI, Buschang PH, Carrillo R, Rossouw PE, Nagy WW, Opperman LA. Histologic evaluation of root response to intrusion in mandibular teeth in beagle dogs. Am J Orthod Dentofacial Orthop. 2011;139(1):60-9.	Excluded; not relevant
99	Reichert C, Kasaj A, Willershausen B. [Orthodontics--periodontics: yesterday and today; a review of the literature]. Schweiz Monatsschr Zahnmed. 2009;119(8):784-91.	Excluded; not relevant
100	Reynders RAM, Ronchi L, Ladu L, van Etten-Jamaludin F, Bipat S. Insertion torque and success of orthodontic mini-implants: A systematic review. American Journal of Orthodontics and Dentofacial Orthopedics. 2012;142(5):596-+.	Excluded; not relevant
101	Reznik DS, Jeske AH, Chen JW, English J. Comparative efficacy of 2 topical anesthetics for the placement of orthodontic temporary anchorage devices. Anesth Prog. 2009;56(3):81-5.	Excluded; not relevant
102	Rodriguez de Guzman-Barrera J, Saez Martinez C, Boronat-Catala M, Montiel-	Excluded; not relevant

	Company JM, Paredes-Gallardo V, Gandia-Franco JL, et al. Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. PLoS One. 2017;12(3):e0173875.	
103	Rodriguez JC, Suarez F, Chan HL, Padial-Molina M, Wang HL. Implants for orthodontic anchorage: success rates and reasons of failures. Implant Dent. 2014;23(2):155-61.	Excluded; not relevant
104	Sabuncuoglu FA, Ersahan S. Changes in maxillary incisor dental pulp blood flow during intrusion by mini-implants. Acta Odontol Scand. 2014;72(7):489-96.	Excluded; not relevant
105	Sarul M, Minch L, Park HS, Antoszewska-Smith J. Effect of the length of orthodontic mini-screw implants on their long-term stability: a prospective study. Angle Orthod. 2015;85(1):33-8.	Excluded; not relevant
106	Schatzle M, Golland D, Roos M, Stawarczyk B. Accuracy of mechanical torque-limiting gauges for mini-screw placement. Clin Oral Implants Res. 2010;21(8):781-8.	Excluded; not relevant
107	Schätzle M, Männchen R, Balbach U, Hämmerle CHF, Toutenburg H, Jung RE. Stability change of chemically modified sandblasted/acid-etched titanium palatal implants. A randomized-controlled clinical trial. Clin Oral Implants Res. 2009;20(5):489-95.	Excluded; not relevant
108	Schatzle M, Mannchen R, Zwahlen M, Lang NP. Survival and failure rates of orthodontic temporary anchorage devices: a systematic review. Clin Oral Implants Res. 2009;20(12):1351-9.	Excluded; not relevant
109	Senisik NE, Turkkahraman H. Treatment effects of intrusion arches and mini-implant systems in deepbite patients. Am J Orthod Dentofacial Orthop. 2012;141(6):723-33.	Excluded; not relevant
110	Shin S, Park PS, Baek SH, Yang IH. Histomorphometric analysis of microcrack healing after the installation of mini-implants. Journal of Periodontal and Implant Science. 2015;45(2):62-8.	Excluded; not relevant
111	Shin YS, Ahn HW, Park YG, Kim SH, Chung KR, Cho IS, et al. Effects of predrilling on the osseointegration potential of mini-implants. Angle Orthod. 2012;82(6):1008-13.	Excluded; not relevant
112	Solano-Mendoza B, Iglesias-Linares A, Yanez-Vico RM, Mendoza-Mendoza A, Alio-Sanz JJ, Solano-Reina E. Maxillary protraction at early ages. The revolution of new bone anchorage appliances. J Clin Pediatr Dent. 2012;37(2):219-29.	Excluded; not relevant
113	Son S, Motoyoshi M, Uchida Y, Shimizu N. Comparative study of the primary stability of self-drilling and self-tapping orthodontic miniscrews. American Journal of Orthodontics and Dentofacial Orthopedics. 2014;145(4):480-5.	Excluded; not relevant
114	Suzuki M, Deguchi T, Watanabe H, Seiryu M, Iikubo M, Sasano T, et al. Evaluation of optimal length and insertion torque for miniscrews. Am J Orthod Dentofacial Orthop. 2013;144(2):251-9.	Excluded; not relevant
115	Turkoz C, Atac MS, Tuncer C, Balos Tuncer B, Kaan E. The effect of drill-free and drilling methods on the stability of mini-implants under early orthodontic loading in adolescent patients. Eur J Orthod. 2011;33(5):533-6.	Excluded; not relevant
116	Ure DS, Oliver DR, Kim KB, Melo AC, Buschang PH. Stability changes of miniscrew implants over time. Angle Orthod. 2011;81(6):994-1000.	Excluded; not relevant
117	Uysal T, Ekizer A, Akcay H, Etoz O, Guray E. Resonance frequency analysis of orthodontic miniscrews subjected to light-emitting diode photobiomodulation therapy. Eur J Orthod. 2012;34(1):44-51.	Excluded; not relevant
118	van Vlijmen OJ, Kuijpers MA, Berge SJ, Schols JG, Maal TJ, Breuning H, et al. Evidence supporting the use of cone-beam computed tomography in orthodontics. J Am Dent Assoc. 2012;143(3):241-52.	Excluded; not relevant
119	Wang DZ, Chen G, Liao YM, Liu SG, Gao ZW, Hu J, et al. A new approach to repairing cleft palate and acquired palatal defects with distraction osteogenesis. Int J Oral Maxillofac Surg. 2006;35(8):718-26.	Excluded; not relevant
120	Winsauer H, Vlachojannis C, Bumann A, Vlachojannis J, Chrubasik S. Paramedian vertical palatal bone height for mini-implant insertion: a systematic review. Eur J Orthod. 2014;36(5):541-9.	Excluded; not relevant
121	Woods PW, Buschang PH, Owens SE, Rossouw PE, Opperman LA. The effect of force, timing, and location on bone-to-implant contact of miniscrew implants. Eur J Orthod. 2009;31(3):232-40.	Excluded; not relevant
122	Wu J, Bai YX, Wang BK. Biomechanical and histomorphometric characterizations of osseointegration during mini-screw healing in rabbit tibiae. Angle Orthod. 2009;79(3):558-63.	Excluded; not relevant
123	Wu Y, Xu Z, Tan L, Zhao Z, Yang P, Li Y, et al. Orthodontic mini-implant stability under continuous or intermittent loading: a histomorphometric and biomechanical analysis. Clin Implant Dent Relat Res. 2015;17(1):163-72.	Excluded; not relevant
124	Yadav S, Upadhyay M, Liu S, Roberts E, Neace WP, Nanda R. Microdamage of the cortical bone during mini-implant insertion with self-drilling and self-tapping techniques: a randomized controlled trial. Am J Orthod Dentofacial Orthop. 2012;141(5):538-46.	Excluded; not relevant
125	Yadav S, Upadhyay M, Roberts WE. Biomechanical and histomorphometric properties of four different mini-implant surfaces. Eur J Orthod. 2015;37(6):627-35.	Excluded; not relevant
126	Yu F, Feng D, Yi Z, Yaling Z, Xiangfeng Z, He Z, et al. [Three-dimensional morphological analysis of corticotomy-assisted intrusion of premolars in Beagle dogs]. Hua Xi Kou Qiang Yi Xue Za Zhi. 2016;34(3):267-71.	Excluded; not relevant
127	Zhang Q, Zhao L, Wu Y, Wang H, Zhao Z, Xu Z, et al. The effect of varying healing times on orthodontic mini-implant stability: a microscopic computerized tomographic and biomechanical analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.	Excluded; not relevant

	2011;112(4):423-9.	
128	Zhao L, Xu Z, Yang Z, Wei X, Tang T, Zhao Z. Orthodontic mini-implant stability in different healing times before loading: a microscopic computerized tomographic and biomechanical analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(2):196-202.	Excluded; not relevant
129	Garfinkle JS, Cunningham LL, Jr., Beeman CS, Kluemper GT, Hicks EP, Kim MO. Evaluation of orthodontic mini-implant anchorage in premolar extraction therapy in adolescents. Am J Orthod Dentofacial Orthop. 2008;133(5):642-53.	Excluded; not relevant
130	Jackson A, Lemke R, Hatch J, Salome N, Gakunga P, Cochran D. A comparison of stability between delayed versus immediately loaded orthodontic palatal implants. Journal of Esthetic and Restorative Dentistry. 2008;20(3):174-84.	Excluded; not relevant
131	Lamberton JA, Oesterle LJ, Shellhart WC, Newman SM, Harrell RE, Tilliss T, et al. Comparison of pain perception during miniscrew placement in orthodontic patients with a visual analog scale survey between compound topical and needle-injected anesthetics: A crossover, prospective, randomized clinical trial. Am J Orthod Dentofacial Orthop. 2016;149(1):15-23.	Excluded; not relevant
132	Lehnen S, McDonald F, Bourauel C, Baxmann M. Patient expectations, acceptance and preferences in treatment with orthodontic mini-implants. A randomly controlled study. Part I: insertion techniques. J Orofac Orthop. 2011;72(2):93-102.	Excluded; not relevant
133	Lehnen S, McDonald F, Bourauel C, Jager A, Baxmann M. Expectations, acceptance and preferences of patients in treatment with orthodontic mini-implants: part II: implant removal. J Orofac Orthop. 2011;72(3):214-22.	Excluded; not relevant
134	Ohashi E, Pecho OE, Moron M, Lagravere MO. Implant vs screw loading protocols in orthodontics: A systematic review. Angle Orthodontist. 2006;76(4):721-7.	Excluded; not relevant
135	Woodall N, Tadepalli SC, Qian F, Grosland NM, Marshall SD, Southard TE. Effect of miniscrew angulation on anchorage resistance. Am J Orthod Dentofacial Orthop. 2011;139(2):e147-52.	Excluded; not relevant
136	Afrashtehfar KI. Patient and miniscrew implant factors influence the success of orthodontic miniscrew implants. Evid Based Dent. 2016;17(4):109-10.	Excluded; no clinical study
137	Al-Dhubhani MK. Modest Evidence Indicates That Orthodontic Force Results in Positional Changes of Orthodontic Miniscrews. Journal of Evidence-Based Dental Practice. 2014;14(3):118-9.	Excluded; no clinical study
138	Bhalla K, Kalha AS. Miniscrew design and bone response: defining a correlation. Orthodontics (Chic). 2013;14(1):e10-21.	Excluded; no clinical study
139	Papadopoulos MA, Papageorgiou SN. Current evidence on clinical performance of miniscrew implants in orthodontic treatment. Seminars in Orthodontics. 2013;19(3):162-73.	Excluded; no clinical study
140	Reynders RM, de Lange J. Moderate quality evidence that surgical anchorage more effective than conventional anchorage during orthodontic treatment. Evid Based Dent. 2014;15(4):108-9.	Excluded; no clinical study
141	Reynders RM. Low quality evidence on the stability of orthodontic mini-implants. Evid Based Dent. 2013;14(3):78-80.	Excluded; no clinical study
142	Sandler PJ. Palatal implants and parental response. Am J Orthod Dentofacial Orthop. 2003;124(4).	Excluded; no clinical study
143	Jung BA, Wehrbein H, Hopfenmuller W, Harzer W, Gedrange T, Diedrich P, et al. Early loading of plalatal implants (ortho-type II) a prospective multicenter randomized controlled clinical trial. Trials. 2007;8:24.	Excluded; no clinical study
144	Antoszewska-Smith J, Sarul M, Lyczek J, Konopka T, Kawala B. Effectiveness of orthodontic miniscrew implants in anchorage reinforcement during en-masse retraction: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017;151(3):440-55.	Systematic review; checked for eligible trials
145	Cornelis MA, Scheffler NR, De Clerck HJ, Tulloch JF, Behets CN. Systematic review of the experimental use of temporary skeletal anchorage devices in orthodontics. Am J Orthod Dentofacial Orthop. 2007;131(4 Suppl):S52-8.	Systematic review; checked for eligible trials
146	Diar-Bakirly S, Feres MF, Saltaji H, Flores-Mir C, El-Bialy T. Effectiveness of the transpalatal arch in controlling orthodontic anchorage in maxillary premolar extraction cases: A systematic review and meta-analysis. Angle Orthod. 2017;87(1):147-58.	Systematic review; checked for eligible trials
147	Grec RH, Janson G, Branco NC, Moura-Grec PG, Patel MP, Castanha Henriques JF. Intraoral distalizer effects with conventional and skeletal anchorage: a meta-analysis. Am J Orthod Dentofacial Orthop. 2013;143(5):602-15.	Systematic review; checked for eligible trials
148	Jambi S, Walsh T, Sandler J, Benson PE, Skeggs RM, O'Brien KD. Reinforcement of anchorage during orthodontic brace treatment with implants or other surgical methods. Cochrane Database Syst Rev. 2014(8):CD005098.	Systematic review; checked for eligible trials
149	Papadopoulos MA, Papageorgiou SN, Zogakis IP. Clinical effectiveness of orthodontic miniscrew implants: a meta-analysis. J Dent Res. 2011;90(8):969-76.	Systematic review; checked for eligible trials
150	Tsui WK, Chua HD, Cheung LK. Bone anchor systems for orthodontic application: a systematic review. Int J Oral Maxillofac Surg. 2012;41(11):1427-38.	Systematic review; checked for eligible trials
151	Fudalej P, Antoszewska J. Are orthodontic distalizers reinforced with the temporary skeletal anchorage devices effective? Am J Orthod Dentofacial Orthop. 2011;139(6):722-9.	Systematic review; checked for eligible trials
152	Li F, Hu HK, Chen JW, Liu ZP, Li GF, He SS, et al. Comparison of anchorage capacity between implant and headgear during anterior segment retraction. Angle Orthod. 2011;81(5):915-22.	Systematic review; checked for eligible trials

153	Wu J, Bai YX, Wang BK, Gao XH. [Stability of the miniscrew implant during healing period]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2006;41(4):226-7.	Excluded; animal study
154	Borsos G, Rudzki-Janson I, Stockmann P, Schlegel KA, Vegh A. Immediate loading of palatal implants in still-growing patients: a prospective, comparative, clinical pilot study. Journal of Orofacial Orthopedics-Fortschritte Der Kieferorthopadie. 2008;69(4):297-308.	Excluded; different intervention to the registered trial
155	Feldmann I, List T, Feldmann H, Bondemark L. Pain intensity and discomfort following surgical placement of orthodontic anchoring units and premolar extraction: a randomized controlled trial. Angle Orthod. 2007;77(4):578-85.	Excluded; different intervention to the registered trial
156	Ganzer N, Feldmann I, Bondemark L. Pain and discomfort following insertion of miniscrews and premolar extractions: A randomized controlled trial. Angle Orthod. 2016;86(6):891-9.	Excluded; different intervention to the registered trial
157	Ozkan S, Bayram M. Comparison of direct and indirect skeletal anchorage systems combined with 2 canine retraction techniques. Am J Orthod Dentofacial Orthop. 2016;150(5):763-70.	Excluded; different intervention to the registered trial
158	Aboul-Ela SM, El-Beialy AR, El-Sayed KM, Selim EM, El-Mangoury NH, Mostafa YA. Miniscrew implant-supported maxillary canine retraction with and without corticotomy-facilitated orthodontics. Am J Orthod Dentofacial Orthop. 2011;139(2):252-9.	Excluded; split-mouth study
159	Crismani AG, Bertl MH, Čelar AG, Bantleon HP, Burstone CJ. Miniscrews in orthodontic treatment: Review and analysis of published clinical trials. American Journal of Orthodontics and Dentofacial Orthopedics. 2010;137(1):108-13.	Excluded; non-eligible outcome
160	Basha AG, Shantaraj R, Mogegowda SB. Comparative study between conventional en-masse retraction (sliding mechanics) and en-masse retraction using orthodontic micro implant. Implant Dent. 2010;19(2):128-36.	Excluded; non-eligible outcome
161	Jung BA, Harzer W, Gedrange T, Kunkel M, Moergel M, Diedrich P, et al. Spectrum of indications for palatal implants in treatment concepts involving immediate and conventional loading. Journal of Orofacial Orthopedics. 2010;71(4):273-80.	Excluded; non-eligible outcome
162	Jung BA, Harzer W, Wehrbein H, Gedrange T, Hopfenmuller W, Ludicke G, et al. Immediate versus conventional loading of palatal implants in humans: a first report of a multicenter RCT. Clin Oral Investig. 2011;15(4):495-502.	Excluded; non-eligible outcome
163	Shi YT, Ping Y, Shan LH, Song JS, Qiu ZX. Stability of mini-implant during orthodontic treatment as anchorage. Journal of clinical rehabilitative tissue engineering research 2008;26:5109-12.	Excluded; non-eligible outcome
164	Victor D, Prabhakar R, Karthikeyan MK, Saravanan R, Vanathi P, Vikram NR, et al. Effectiveness of mini implants in three-dimensional control during retraction - a clinical study. J Clin Diagn Res. 2014;8(2):227-32.	Excluded; non-eligible outcome
165	Al-Sibaie S, Hajeer MY. Assessment of changes following en-masse retraction with mini-implants anchorage compared to two-step retraction with conventional anchorage in patients with class II division 1 malocclusion: a randomized controlled trial. Eur J Orthod. 2014;36(3):275-83.	Included for potential evaluation
166	Benson PE, Tinsley D, O'Dwyer JJ, Majumdar A, Doyle P, Sandler PJ. Midpalatal implants vs headgear for orthodontic anchorage - a randomized clinical trial: Cephalometric results. American Journal of Orthodontics and Dentofacial Orthopedics. 2007;132(5):606-15.	Included for potential evaluation
167	Feldmann I, Bondemark L. Anchorage capacity of osseointegrated and conventional anchorage systems: a randomized controlled trial. Am J Orthod Dentofacial Orthop. 2008;133(3):339 e19-28.	Included for potential evaluation
168	Feldmann I, List T, Bondemark L. Orthodontic anchoring techniques and its influence on pain, discomfort, and jaw function--a randomized controlled trial. Eur J Orthod. 2012;34(1):102-8.	Included for potential evaluation
169	Feldmann I. Orthodontic anchorage--Evidence-based evaluation of anchorage capacity and patients' perceptions. Swed Dent J Suppl. 2007(191):10-86.	Included for potential evaluation
170	Liu YH, Ding WH, Liu J, Li Q. Comparison of the differences in cephalometric parameters after active orthodontic treatment applying mini-screw implants or transpalatal arches in adult patients with bialveolar dental protrusion. J Oral Rehabil. 2009;36(9):687-95.	Included for potential evaluation
171	Sandler J, Benson PE, Doyle P, Majumder A, O'Dwyer J, Speight P, et al. Palatal implants are a good alternative to headgear: A randomized trial. American Journal of Orthodontics and Dentofacial Orthopedics. 2008;133(1):51-7.	Included for potential evaluation
172	Sandler J, Murray A, Thiruvenkatachari B, Gutierrez R, Speight P, O'Brien K. Effectiveness of 3 methods of anchorage reinforcement for maximum anchorage in adolescents: A 3-arm multicenter randomized clinical trial. Am J Orthod Dentofacial Orthop. 2014;146(1):10-20.	Included for potential evaluation
173	Sharma M, Sharma V, Khanna B. Mini-screw implant or transpalatal arch-mediated anchorage reinforcement during canine retraction: a randomized clinical trial. J Orthod. 2012;39(2):102-10.	Included for potential evaluation
174	Upadhyay M, Yadav S, Nagaraj K, Patil S. Treatment effects of mini-implants for en-masse retraction of anterior teeth in bialveolar dental protrusion patients: A randomized controlled trial. American Journal of Orthodontics and Dentofacial Orthopedics. 2008a;134(1):18-29.e1.	Included for potential evaluation
175	Upadhyay M, Yadav S, Patil S. Mini-implant anchorage for en-masse retraction of maxillary anterior teeth: a clinical cephalometric study. Am J Orthod Dentofacial Orthop. 2008b;134(6):803-10.	Included for potential evaluation

176	Ma N, Li WR, Chen XH, Zheng X. [Comparison of treatment results between implant anchorage and traditional intraoral anchorage in patients with maxillary protrusion]. Shanghai Kou Qiang Yi Xue. 2016 Aug;25(4):475-480.	Included for potential evaluation
177	Yu SD, Hong XC, Yao QH, et al. Clinical comparison between micro-screw implant and headgear used for anchorage control. J Dent Prev Treat. 2011;19(8):414–416.	Included for potential evaluation
178	Huang XF, Han PY. Comparison of clinical effects between screw-implant and extra-force as anchorage. Beijing J Stomatol. 2007;15:213–215.	Included for potential evaluation
179	Wei MG, Lu DZ, Wang GS. Comparison of micro-implant anchorage with headgear anchorage in treatment of maxillary dentoalveolar protrusion. J Tong Ji University. 2011;32:52–56.	Included for potential evaluation
180	Su QZ, Yan Y, Yan HY. Comparison of clinical effects between microscrew implant and headgear in control. Chin J Orthod. 2009;16:140–143.	Included for potential evaluation
181	Gokce SM, Gorgulu S, Gokce HS, Yildirim E, Sagdic D. Comparison of conventional molar tooth anchorage and micro-implant anchorage regarding canine retraction in treatments with extraction. Gulhane Med J. 2012;54:205–211.	Included for potential evaluation

Supplementary Table 3f. List of included/excluded studies on the topic of gum as adjunct.

Nr.	Paper	Status
1	Abdullah Z, John J. Minimally Invasive Treatment of White Spot Lesions - A Systematic Review. Oral Health & Preventive Dentistry. 2016;14(3):197-205.	Excluded; screening of title
2	Antonio AG, Pierro VS, Maia LC. Caries preventive effects of xylitol-based candies and lozenges: a systematic review. J Public Health Dent. 2011;71(2):117-24.	Excluded; screening of title
3	Bailey DL, Adams GG, Tsao CE, Hyslop A, Escobar K, Manton DJ, et al. Regression of Post-orthodontic Lesions by a Remineralizing Cream. J Dent Res. 2009;88(12):1148-53.	Excluded; screening of title
4	Bhatka R, Throckmorton GS, Wintergerst AM, Hutchins B, Buschang PH. Bolus size and unilateral chewing cycle kinematics. Arch Oral Biol. 2004;49(7):559-66.	Excluded; screening of title
5	Buschang PH, Hayasaki H, Throckmorton GS. Quantification of human chewing-cycle kinematics. Arch Oral Biol. 2000;45(6):461-74.	Excluded; screening of title
6	Ellis PE, Bradley RL, Sandy JR, Deacon SA, Griffiths HS, Atack NE, et al. Do I have enough time? The impact of recruiting patients to a randomised controlled trial at recruiting centres. Br Dent J. 2012;213(9):467-70.	Excluded; screening of title
7	Farella M, Bakke M, Michelotti A, Martina R. Effects of prolonged gum chewing on pain and fatigue in human jaw muscles. Eur J Oral Sci. 2001;109(2):81-5.	Excluded; screening of title
8	Ghasempour M, Sefdgar SA, Moghadamnia AA, Ghadimi R, Gharekhani S, Shirkhani L. Comparative study of Kefir yogurt-drink and sodium fluoride mouth rinse on salivary mutans streptococci. The journal of contemporary dental practice. 2014;15(2):214-7.	Excluded; screening of title
9	Heymann GC, Grauer D. A Contemporary Review of White Spot Lesions in Orthodontics. Journal of Esthetic and Restorative Dentistry. 2013;25(2):85-95.	Excluded; screening of title
10	Holgerson PL, Stecksen-Blinks C, Sjostrom I, Twetman S. Effect of xylitol-containing chewing gums on interdental plaque-pH in habitual xylitol consumers. Acta Odontologica Scandinavica. 2005;63(4):233-8.	Excluded; screening of title
11	Huang GJ, Roloff-Chiang B, Mills BE, Shalchi S, Spiekerman C, Korpak AM, et al. Effectiveness of MI Paste Plus and PreviDent fluoride varnish for treatment of white spot lesions: A randomized controlled trial. American Journal of Orthodontics and Dentofacial Orthopedics. 2013;143(1):31-41.	Excluded; screening of title
12	Jain A, Bhaskar DJ, Gupta D, Agali C, Gupta V, Gupta RK, et al. Comparative evaluation of honey, chlorhexidine gluconate (0.2%) and combination of xylitol and chlorhexidine mouthwash (0.2%) on the clinical level of dental plaque: A 30 days randomized control trial. Perspect Clin Res. 2015;6(1):53-7.	Excluded; screening of title
13	Li JL, Xie XQ, Wang Y, Yin W, Antoun JS, Farella M, et al. Long-term remineralizing effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on early caries lesions in vivo: A systematic review. J Dent. 2014;42(7):769-77.	Excluded; screening of title
14	Macfarlane TV, Gray RJM, Kincey J, Worthington HV. Factors associated with the temporomandibular disorder, pain dysfunction syndrome (PDS): Manchester case-control study. Oral Dis. 2001;7(6):321-30.	Excluded; screening of title
15	Nayak UA, Sharma R, Kashyap N, Prajapati D, Kappadi D, Wadhwa S, et al. Association between Chewing Side Preference and Dental Caries among Deciduous, Mixed and Permanent Dentition. J Clin Diagn Res. 2016;10(9):ZC05-ZC8.	Excluded; screening of title
16	Ohmure H, Takada H, Nagayama K, Sakiyama T, Tsubouchi H, Miyawaki S. Mastication suppresses initial gastric emptying by modulating gastric activity. J Dent Res. 2012;91(3):293-8.	Excluded; screening of title
17	Park SY, Cha JY, Kim KN, Hwang CJ. The effect of casein phosphopeptide amorphous calcium phosphate on the in vitro shear bond strength of orthodontic brackets. Korean Journal of Orthodontics. 2013;43(1):23-8.	Excluded; screening of title
18	Popescu SM, Dascalu IT, Scrieciu M, Mercut V, Moraru I, Tuculina MJ. Dental Anxiety and its Association with Behavioral Factors in Children. Curr Health Sci J. 2014;40(4):261-4.	Excluded; screening of title
19	Rios D, Honorio HM, Magalhaes AC, Delbem AC, Machado MA, Silva SM, et al. Effect of salivary stimulation on erosion of human and bovine enamel subjected or not to subsequent abrasion: an in situ/ex vivo study. Caries Res. 2006;40(3):218-23.	Excluded; screening of title
20	Saeed S, Bshara N, Trak J, Mahmoud G. Effect of dietary combinations on plaque pH recovery after the intake of pediatric liquid analgesics. Eur J Dent. 2015;9(3):340-5.	Excluded; screening of title
21	Sever E, Marion L, Ovsenik M. Relationship between masticatory cycle morphology and unilateral crossbite in the primary dentition. European Journal of Orthodontics. 2011;33(6):620-7.	Excluded; screening of title
22	Splieth CH, Alkilzy M, Schmitt J, Berndt C, Welk A. Effect of xylitol and sorbitol on plaque acidogenesis. Quintessence International. 2009;40(4):279-85.	Excluded; screening of title
23	Sudjalim TR, Woods MG, Manton DJ, Reynolds EC. Prevention of demineralization around orthodontic brackets in vitro. American Journal of Orthodontics and Dentofacial Orthopedics. 2007;131(6).	Excluded; screening of title
24	Veli I, Akin M, Baka ZM, Uysal T. Effects of different pre-treatment methods on the shear bond strength of orthodontic brackets to demineralized enamel. Acta Odontologica Scandinavica. 2016;74(1):7-13.	Excluded; screening of title
25	Willmot D. White Spot Lesions After Orthodontic Treatment. Seminars in Orthodontics. 2008;14(3):209-19.	Excluded; screening of title
26	Wintergerst AM, Buschang PH, Hutchins B, Throckmorton GS. Effect of an auditory cue on chewing cycle kinematics. Arch Oral Biol. 2006;51(1):50-7.	Excluded; screening of title
27	de Alencar CR, Magalhaes AC, de Andrade Moreira Machado MA, de Oliveira TM, Honorio HM, Rios D. In situ effect of a commercial CPP-ACP chewing gum on the human enamel initial erosion. J Dent. 2014;42(11):1502-7.	Excluded; screening of abstract
28	Ding XJ, Lu J, Guo XH, Ruan H, Yu YC, Gu ZY, et al. Effects of CPP-ACP Paste on the Shear Bond Strength of Orthodontic Brackets. Angle Orthodontist. 2009;79(5):945-50.	Excluded; screening of

		abstract
29	Gray A, Ferguson MM. The use of low-tack chewing gum for individuals wearing orthodontic appliances. Aust Dent J. 1996;41(6):373-6.	Excluded; screening of abstract
30	Jordao MC, Alencar CR, Mesquita IM, Buzalaf MA, Magalhaes AC, Machado MA, et al. In situ Effect of Chewing Gum with and without CPP-ACP on Enamel Surface Hardness Subsequent to ex vivo Acid Challenge. Caries Res. 2016;50(3):325-30.	Excluded; screening of abstract
31	Khoroushi M, Kachuie M. Prevention and Treatment of White Spot Lesions in Orthodontic Patients. Contemporary Clinical Dentistry. 2017;8(1):11-9.	Excluded; screening of abstract
32	Paula VA, Modesto A, Santos KR, Gleiser R. Antimicrobial effects of the combination of chlorhexidine and xylitol. Br Dent J. 2010;209(12):E19.	Excluded; screening of abstract
33	Sultan S, Telgi CR, Chaudhary S, Manuja N, Kaur H, Amit SA, Lingesha RT. Effect of ACP-CPP Chewing Gum and Natural Chewable Products on Plaque pH, Calcium and Phosphate Concentration. J Clin Diagn Res. 2016 Apr;10(4):ZC13-7.	Excluded; screening of abstract
34	Uysal T, Baysal A, Uysal B, Aydinbelge M, Al-Qunaian T. Do fluoride and casein phosphopeptide-amorphous calcium phosphate affect shear bond strength of orthodontic brackets bonded to a demineralized enamel surface? Angle Orthodontist. 2011;81(3):490-5.	Excluded; screening of abstract
35	Yap J, Walsh LJ, Naser-ud Din S, Ngo H, Manton DJ. Evaluation of a novel approach in the prevention of white spot lesions around orthodontic brackets. Aust Dent J. 2014;59(1):70-80.	Excluded; screening of abstract
36	Fleming PS, Strydom H, Katsaros C, MacDonald L, Curatolo M, Fudalej P, et al. Non-pharmacological interventions for alleviating pain during orthodontic treatment. Cochrane Database Syst Rev. 2016;12:CD010263.	Systematic review; checked for eligible trials
37	Goldreich H, Gazit E, Lieberman MA, Rugh JD. The effect of pain from orthodontic arch wire adjustment on masseter muscle electromyographic activity. Am J Orthod Dentofacial Orthop. 1994;106(4):365-70.	Excluded; no randomisation
38	Cosyn J, Verelst K. An efficacy and safety analysis of a chlorhexidine chewing gum in young orthodontic patients. J Clin Periodontol. 2006;33(12):894-9.	Excluded; different intervention to the registered trial
39	Isotupa KP, Gunn S, Chen CY, Lopatin D, Makinen KK. Effect of polyol gums on dental plaque in orthodontic patients. Am J Orthod Dentofacial Orthop. 1995;107(5):497-504.	Excluded; different intervention to the registered trial
40	Stecksen-Blicks C, Holgerson PL, Olsson M, Bylund B, Sjostrom I, Skold-Larsson K, et al. Effect of xylitol on mutans streptococci and lactic acid formation in saliva and plaque from adolescents and young adults with fixed orthodontic appliances. Eur J Oral Sci. 2004;112(3):244-8.	Excluded; different intervention to the registered trial
41	Masoud MI, Allarakia R, Alamoudi NM, Nalliah R, Allareddy V. Long-term clinical and bacterial effects of xylitol on patients with fixed orthodontic appliances. Prog Orthod. 2015;16:35.	Excluded; non-eligible outcome
42	Benson PE, Razi RM, Al-Bloushi RJ. The effect of chewing gum on the impact, pain and breakages associated with fixed orthodontic appliances: a randomized clinical trial. Orthod Craniofac Res. 2012;15(3):178-87.	Included for potential evaluation
43	Farzanegan F, Zebarjad SM, Alizadeh S, Ahrari F. Pain reduction after initial archwire placement in orthodontic patients: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2012;141(2):169-73.	Included for potential evaluation
44	Ireland AJ, Ellis P, Jordan A, Bradley R, Ewings P, Atack NE, et al. Chewing gum vs. ibuprofen in the management of orthodontic pain, a multi-centre randomised controlled trial - the effect of anxiety. J Orthod. 2017;44(1):3-7.	Included for potential evaluation
45	Ireland AJ, Ellis P, Jordan A, Bradley R, Ewings P, Atack NE, et al. Comparative assessment of chewing gum and ibuprofen in the management of orthodontic pain with fixed appliances: A pragmatic multicenter randomized controlled trial. Am J Orthod Dentofacial Orthop. 2016;150(2):220-7.	Included for potential evaluation
46	Nadeem M, Tariq J, Kamran MA, Mahroof V, Siddique R, Batool F, Qamruddin I. Effect of Chewing Gum on Pain in Fixed Orthodontic Treatment. ASH & KMDC 2016;21(2):94.	Included for potential evaluation
47	Shedam, M. The Effect of Chewing Gum on the Pain Associated With Initial Placement of Fixed Orthodontic Appliances. (2015) J Dent & Oral Care 1(1): 1- 4.	Included for potential evaluation

Supplementary Table 3g. List of included/excluded studies on the topic of low level light therapy.

Nr.	Paper	Status
1	Abi-Ramia LB, Stuani AS, Stuani MB, Mendes Ade M. Effects of low-level laser therapy and orthodontic tooth movement on dental pulps in rats. Angle Orthod. 2010;80(1):116-22.	Excluded; screening of title
2	Abtahi M, Poosti M, Saghravanian N, Sadeghi K, Shafaee H. The effect of low level laser on condylar growth during mandibular advancement in rabbits. Head Face Med. 2012;8:4.	Excluded; screening of title
3	Akpinar YZ, Irgin C, Yavuz T, Aslan MA, Kilic HS, Usumez A. Effect of femtosecond laser treatment on the shear bond strength of a metal bracket to prepared porcelain surface. Photomed Laser Surg. 2015;33(4):206-12.	Excluded; screening of title
4	Alsulaimani M, Doschak M, Dederich D, Flores-Mir C. Effect of low-level laser therapy on dental root cementum remodeling in rats. Orthod Craniofac Res. 2015;18(2):109-16.	Excluded; screening of title
5	Bidar M, Moushekhian S, Gharechahi M, Talati A, Ahrari F, Bojarpour M. The Effect of Low Level Laser Therapy on Direct Pulp Capping in Dogs. J Lasers Med Sci. 2016;7(3):177-83.	Excluded; screening of title
6	Cadenas-Perula M, Yanez-Vico RM, Solano-Reina E, Iglesias-Linares A. Effectiveness of biologic methods of inhibiting orthodontic tooth movement in animal studies. Am J Orthod Dentofacial Orthop. 2016;150(1):33-48.	Excluded; screening of title
7	Camacho AD, Velasquez Cujar SA. Dental movement acceleration: Literature review by an alternative scientific evidence method. World J Methodol. 2014;4(3):151-62.	Excluded; screening of title
8	Cepera F, Torres FC, Scanavini MA, Paranhos LR, Capelozza Filho L, Cardoso MA, et al. Effect of a low-level laser on bone regeneration after rapid maxillary expansion. Am J Orthod Dentofacial Orthop. 2012;141(4):444-50.	Excluded; screening of title
9	da Silva Neves FL, Silveira CA, Dias SB, Santamaria Junior M, de Marco AC, Kerbauy WD, et al. Comparison of two power densities on the healing of palatal wounds after connective tissue graft removal: randomized clinical trial. Lasers Med Sci. 2016;31(7):1371-8.	Excluded; screening of title
10	Dionysopoulos D, Strakas D, Tsitrou E, Tolidis K, Koumpia E. Effect of Er,Cr:YSGG laser on the surface of composite restoratives during in-office tooth bleaching. Lasers Med Sci. 2016;31(5):875-82.	Excluded; screening of title
11	Duan J, Na Y, Liu Y, Zhang Y. Effects of the pulse frequency of low-level laser therapy on the tooth movement speed of rat molars. Photomed Laser Surg. 2012;30(11):663-7.	Excluded; screening of title
12	Eshghpour M, Ahrari F, Takallu M. Is Low-Level Laser Therapy Effective in the Management of Pain and Swelling After Mandibular Third Molar Surgery? J Oral Maxillofac Surg. 2016;74(7):1322 e1-8.	Excluded; screening of title
13	Eshghpour M, Shaban B, Ahrari F, Erfanian M, Shadkam E. Is Low-Level Laser Therapy Effective for Treatment of Neurosensory Deficits Arising From Sagittal Split Ramus Osteotomy? J Oral Maxillofac Surg. 2017.	Excluded; screening of title
14	Fekrazad R, Eslaminejad MB, Shayan AM, Kalhori KA, Abbas FM, Taghiyar L, et al. Effects of Photobiomodulation and Mesenchymal Stem Cells on Articular Cartilage Defects in a Rabbit Model. Photomed Laser Surg. 2016;34(11):543-9.	Excluded; screening of title
15	Feres MFN, Kucharski C, Diar-Bakirly S, El-Bialy T. Effect of low-intensity pulsed ultrasound on the activity of osteoclasts: An in vitro study. Arch Oral Biol. 2016;70:73-8.	Excluded; screening of title
16	Franzen TJ, Zahra SE, El-Kadi A, Vandevska-Radunovic V. The influence of low-level laser on orthodontic relapse in rats. Eur J Orthod. 2015;37(1):111-7.	Excluded; screening of title
17	Garcia VJ, Arnabat J, Comesana R, Kasem K, Ustrell JM, Pasetto S, et al. Effect of low-level laser therapy after rapid maxillary expansion: a clinical investigation. Lasers Med Sci. 2016;31(6):1185-94.	Excluded; screening of title
18	Gasperini G, Rodrigues de Siqueira IC, Rezende Costa L. Does low-level laser therapy decrease swelling and pain resulting from orthognathic surgery? Int J Oral Maxillofac Surg. 2014;43(7):868-73.	Excluded; screening of title
19	Giannasi LC, Matsui MY, de Freitas Batista SR, Hardt CT, Gomes CP, Amorim JB, et al. Effects of neuromuscular electrical stimulation, laser therapy and LED therapy on the masticatory system and the impact on sleep variables in cerebral palsy patients: a randomized, five arms clinical trial. BMC Musculoskelet Disord. 2012;13:71.	Excluded; screening of title
20	Godoy BM, Arana-Chavez VE, Nunez SC, Ribeiro MS. Effects of low-power red laser on dentine-pulp interface after cavity preparation. An ultrastructural study. Arch Oral Biol. 2007;52(9):899-903.	Excluded; screening of title
21	Habib FA, Gama SK, Ramalho LM, Cangussu MC, dos Santos Neto FP, Lacerda JA, et al. Effect of laser phototherapy on the hyalinization following orthodontic tooth movement in rats. Photomed Laser Surg. 2012;30(3):179-85.	Excluded; screening of title
22	Han KH, Park JH, Bayome M, Jeon IS, Lee W, Kook YA. Effect of Frequent Application of Low-Level Laser Therapy on Corticotomized Tooth Movement in Dogs: A Pilot Study. Journal of Oral and Maxillofacial Surgery. 2014;72(6).	Excluded; screening of title
23	Hayashi H, Terao A, Kunimatsu R, Kawata T. Effects of a low level laser on periodontal tissue in hypofunctional teeth. PLoS One. 2014;9(6):e100066.	Excluded; screening of title
24	Higashi DT, Andrello AC, Tondelli PM, de Oliveira Toginho Filho D, de Paula Ramos S. Three consecutive days of application of LED therapy is necessary to inhibit experimentally induced root resorption in rats: a microtomographic study. Lasers Med Sci. 2017;32(1):181-7.	Excluded; screening of title
25	Marques NC, Neto NL, Rodini Cde O, Fernandes AP, Sakai VT, Machado MA, et al. Low-level laser therapy as an alternative for pulpotomy in human primary teeth. Lasers Med Sci. 2015;30(7):1815-22.	Excluded; screening of title
26	Momenzadeh S, Akhyani V, Razaghi Z, Ebadifar A, Abbasi M. Evaluation of the Effects of Intravenous and Percutaneous Low Level Laser Therapy in the Management of Shoulder Myofascial Pain Syndrome. J Lasers Med Sci. 2016;7(1):16-20.	Excluded; screening of title

27	Qamruddin I, Alam MK, Khamis MF, Husein A. Minimally Invasive Techniques to Accelerate the Orthodontic Tooth Movement: A Systematic Review of Animal Studies. Biomed Res Int. 2015;2015:608530.	Excluded; screening of title
28	Oksayan R, Sokucu O, Ucuncu N. The effects of low-level laser therapy on condylar growth with a mandibular advancement appliance in rats. Photomed Laser Surg. 2015;33(5):252-7.	Excluded; screening of title
29	Rechmann P, Fried D, Le CQ, Nelson G, Rapozo-Hilo M, Rechmann BM, et al. Caries inhibition in vital teeth using 9.6-mum CO2-laser irradiation. J Biomed Opt. 2011;16(7):071405.	Excluded; screening of title
30	Santiago VCCE, Piram A, Fuziy A. Effect of soft laser in bone repair after expansion of the midpalatal suture in dogs. American Journal of Orthodontics and Dentofacial Orthopedics. 2012;142(5):615-24.	Excluded; screening of title
31	Santinoni CD, Oliveira HF, Batista VE, Lemos CA, Verri FR. Influence of low-level laser therapy on the healing of human bone maxillofacial defects: A systematic review. J Photochem Photobiol B. 2017;169:83-9.	Excluded; screening of title
32	Seifi M, Atri F, Yazdani MM. Effects of low-level laser therapy on orthodontic tooth movement and root resorption after artificial socket preservation. Dent Res J (Isfahan). 2014;11(1):61-6.	Excluded; screening of title
33	Seifi M, Maghzi A, Gutknecht N, Mir M, Asna-Ashari M. The effect of 904 nm low level laser on condylar growth in rats. Lasers Med Sci. 2010;25(1):61-5.	Excluded; screening of title
34	Shirazi M, Ahmad Akhoundi MS, Javadi E, Kamali A, Motahhari P, Rashidpour M, et al. The effects of diode laser (660 nm) on the rate of tooth movements: an animal study. Lasers Med Sci. 2015;30(2):713-8.	Excluded; screening of title
35	Silva LC, Sacono NT, Freire Mdo C, Costa LR, Batista AC, Silva GB. The Impact of Low-Level Laser Therapy on Oral Mucositis and Quality of Life in Patients Undergoing Hematopoietic Stem Cell Transplantation Using the Oral Health Impact Profile and the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation Questionnaires. Photomed Laser Surg. 2015;33(7):357-63.	Excluded; screening of title
36	Silva TC, Oliveira TM, Sakai VT, Dionisio TJ, Santos CF, Bagnato VS, et al. In vivo effects on the expression of vascular endothelial growth factor-A165 messenger ribonucleic acid of an infrared diode laser associated or not with a visible red diode laser. Photomed Laser Surg. 2010;28(1):63-8.	Excluded; screening of title
37	Sobouti F, Rakhshan V, Chiniforush N, Khatami M. Effects of laser-assisted cosmetic smile lift gingivectomy on postoperative bleeding and pain in fixed orthodontic patients: A controlled clinical trial. Prog Orthod. 2014;15(1).	Excluded; screening of title
38	Topcuoglu T, Oksayan R, Topcuoglu S, Coskun ME, Isman NE. Effect of Er:YAG laser pulse duration on shear bond strength of metal brackets bonded to a porcelain surface. Photomed Laser Surg. 2013;31(6):240-6.	Excluded; screening of title
39	Zahra SE, Elkasi AA, Eldin MS, Vandevska-Radunovic V. The effect of low level laser therapy (LLLT) on bone remodelling after median diastema closure: A one year and half follow-up study. Orthodontic Waves. 2009;68(3):116-22.	Excluded; screening of title
40	Zhu X, Chen Y, Sun X. [A study on expression of basic fibroblast growth factors in periodontal tissue following orthodontic tooth movement associated with low power laser irradiation]. Hua Xi Kou Qiang Yi Xue Za Zhi. 2002;20(3):166-8.	Excluded; screening of title
41	Cakir-Ozkan N, Bereket C, Arici N, Elmali M, Sener I, Bekar E. The Radiological and Stereological Analysis of the Effect of Low-Level Laser Therapy on the Mandibular Midline Distraction Osteogenesis. J Craniofac Surg. 2015;26(7):e595-9.	Excluded; screening of title
42	Chan A, Armati P, Moorthy AP. Pulsed Nd: YAG laser induces pulpal analgesia: a randomized clinical trial. J Dent Res. 2012;91(7 Suppl):79S-84S.	Excluded; screening of title
43	Kim KA, Choi EK, Ohe JY, Ahn HW, Kim SJ. Effect of low-level laser therapy on orthodontic tooth movement into bone-grafted alveolar defects. Am J Orthod Dentofacial Orthop. 2015;148(4):608-17.	Excluded; screening of title
44	Abdallah MN, Flores-Mir C. Are interventions for accelerating orthodontic tooth movement effective? Evid Based Dent. 2014;15(4):116-7.	Excluded; screening of abstract
45	Consolaro A. Effects of medications and laser on induced tooth movement and associated root resorption: Four key points. Dental Press J Orthod. 2013;18(2):4-7.	Excluded; screening of abstract
46	Farsaii A, Al-Jewair T. Insufficient Evidence Supports the Use of Low-Level Laser Therapy to Accelerate Tooth Movement, Prevent Orthodontic Relapse, and Modulate Acute Pain During Orthodontic Treatment. Journal of Evidence-Based Dental Practice. 2017.	Excluded; screening of abstract
47	Fleming PS. Accelerating orthodontic tooth movement using surgical and non-surgical approaches. Evid Based Dent. 2014;15(4):114-5.	Excluded; screening of abstract
48	He W, Li C, Zou S. Reply to comments on: "Efficacy of low-level laser therapy in the management of orthodontic pain: a systematic review and meta-analysis". Lasers Med Sci. 2015;30(2):941-2.	Excluded; screening of abstract
49	Long H, Wang Y, Jian F, Liao LN, Yang X, Lai WL. Current advances in orthodontic pain. International Journal of Oral Science. 2016;8(2):67-75.	Excluded; screening of abstract
50	Nimeri G, Kau CH, Abou-Kheir NS, Corona R. Acceleration of tooth movement during orthodontic treatment - a frontier in Orthodontics. Prog Orthod. 2013;14(1):1-8.	Excluded; screening of abstract
51	Rozen D, Khoo E, Sayed HE, Niederman R, McGowan R, Alikhani M, et al. Accelerated tooth movement: Do we need a new systematic review? Seminars in Orthodontics. 2015;21(3):224-30.	Excluded; screening of abstract
52	Yan B. Comments on: "efficacy of low-level laser therapy in the management of orthodontic pain: a systematic review and meta-analysis". Lasers Med Sci. 2014;29(4):1531.	Excluded; screening of abstract
53	Carroll JD. Tooth movement in orthodontic treatment systematic review omitted significant articles. Photomed Laser Surg. 2014;32(5):310-1.	Excluded; screening of abstract

54	Dominguez A, Velasquez SA. Tooth movement in orthodontic treatment with low-level laser therapy: systematic review imprecisions. Photomed Laser Surg. 2014;32(8):476-7.	Excluded; screening of abstract
55	Shaughnessy T, Kantarci A, Kau CH, Skrenes D, Skrenes S, Ma D. Intraoral photobiomodulation-induced orthodontic tooth alignment: a preliminary study. BMC Oral Health. 2016;16.	Excluded; no randomisation
56	Kim SJ, Moon SU, Kang SG, Park YG. Effects of low-level laser therapy after Corticision on tooth movement and paradental remodeling. Lasers Surg Med. 2009;41(7):524-33.	Excluded; different intervention to the registered trial
57	Devi A, Sathyanarayana HP, Kailasam V. Re: Evaluation of the use of low-level laser therapy in pain control in orthodontic patients: A randomized split-mouth clinical trial. The Angle Orthodontist. 2016; 86:193-198. Angle Orthodontist. 2016;86(6):1058-.	Excluded; split-mouth study
58	Sobouti F, Khatami M, Chiniforush N, Rakhshan V, Shariati M. Effect of single-dose low-level helium-neon laser irradiation on orthodontic pain: a split-mouth single-blind placebo-controlled randomized clinical trial. Prog Orthod. 2015;16:32.	Excluded; split-mouth study
59	Abellan R, Gomez C, Oteo MD, Scuzzo G, Palma JC. Short- and Medium-Term Effects of Low-Level Laser Therapy on Periodontal Status in Lingual Orthodontic Patients. Photomed Laser Surg. 2016;34(7):284-90.	Excluded; split-mouth study
60	Almallah MM, Almahdi WH, Hajeer MY. Evaluation of Low Level Laser Therapy on Pain Perception Following Orthodontic Elastomeric Separation: A Randomized Controlled Trial. J Clin Diagn Res. 2016;10(11):ZC23-ZC8.	Excluded; split-mouth study
61	Artes-Ribas M, Arnabat-Dominguez J, Puigdollers A. Analgesic effect of a low-level laser therapy (830 nm) in early orthodontic treatment. Lasers Med Sci. 2013;28(1):335-41.	Excluded; split-mouth study
62	Bicakci AA, Kocoglu-Altan B, Toker H, Mutaf I, Sumer Z. Efficiency of low-level laser therapy in reducing pain induced by orthodontic forces. Photomed Laser Surg. 2012;30(8):460-5.	Excluded; split-mouth study
63	Dominguez A, Velasquez SA. Effect of low-level laser therapy on pain following activation of orthodontic final archwires: a randomized controlled clinical trial. Photomed Laser Surg. 2013;31(1):36-40.	Excluded; split-mouth study
64	Ureturk SE, Sarac M, Firatli S, Can SB, Guven Y, Firatli E. The effect of low-level laser therapy on tooth movement during canine distalization. Lasers Med Sci. 2017;32(4):757-64.	Excluded; split-mouth study
65	Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: a clinical investigation. Am J Orthod Dentofacial Orthop. 2012;141(3):289-97.	Excluded; split-mouth study
66	Eslamian L, Borzabadi-Farahani A, Hassanzadeh-Azhiri A, Badiee MR, Fekrazad R. The effect of 810-nm low-level laser therapy on pain caused by orthodontic elastomeric separators. Lasers Med Sci. 2014;29(2):559-64.	Excluded; split-mouth study
67	Farias RD, Closs LQ, Miguens SA, Jr. Evaluation of the use of low-level laser therapy in pain control in orthodontic patients: A randomized split-mouth clinical trial. Angle Orthod. 2016;86(2):193-8.	Excluded; split-mouth study
68	Dalaie K, Hamedi R, Kharazifard MJ, Mahdian M, Bayat M. Effect of Low-Level Laser Therapy on Orthodontic Tooth Movement: A Clinical Investigation. J Dent (Tehran). 2015;12(4):249-56.	Excluded; split-mouth study
69	Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. Orthod Craniofac Res. 2006;9(1):38-43.	Excluded; split-mouth study
70	Yassaei S, Aghili H, Afshari JT, Bagherpour A, Eslami F. Effects of diode laser (980 nm) on orthodontic tooth movement and interleukin 6 levels in gingival crevicular fluid in female subjects. Lasers Med Sci. 2016;31(9):1751-9.	Excluded; split-mouth study
71	Xiaoting L, Yin T, Yangxi C. Interventions for pain during fixed orthodontic appliance therapy. A systematic review. Angle Orthod. 2010;80(5):925-32.	Excluded; non-eligible outcome
72	AlSayed Hasan MMA, Sultan K, Hamadah O. Evaluating low-level laser therapy effect on reducing orthodontic pain using two laser energy values: a split-mouth randomized placebo-controlled trial. Eur J Orthod. 2017.	Excluded; non-eligible outcome
73	Bayani S, Rostami S, Ahrari F, Saeedipouya I. A randomized clinical trial comparing the efficacy of bite wafer and low level laser therapy in reducing pain following initial arch wire placement. Laser Ther. 2016;25(2):121-9.	Excluded; non-eligible outcome
74	Eslamipour F, Motamedian SR, Bagheri F. Ibuprofen and Low-level Laser Therapy for Pain Control during Fixed Orthodontic Therapy: A Systematic Review of Randomized Controlled Trials and Meta-analysis. J Contemp Dent Pract. 2017;18(6):527-33.	Excluded; non-eligible outcome
75	Esper MA, Nicolau RA, Arisawa EA. The effect of two phototherapy protocols on pain control in orthodontic procedure--a preliminary clinical study. Lasers Med Sci. 2011;26(5):657-63.	Excluded; non-eligible outcome
76	Furquim RD, Pascotto RC, Rino Neto J, Cardoso JR, Ramos AL. Low-level laser therapy effects on pain perception related to the use of orthodontic elastomeric separators. Dental Press J Orthod. 2015;20(3):37-42.	Excluded; non-eligible outcome
77	He WL, Li CJ, Liu ZP, Sun JF, Hu ZA, Yin X, et al. Efficacy of low-level laser therapy in the management of orthodontic pain: a systematic review and meta-analysis. Lasers Med Sci. 2013;28(6):1581-9.	Excluded; non-eligible outcome
78	Jahanbin A, Ramazanzadeh B, Ahrari F, Forouzanfar A, Beidokhti M. Effectiveness of Er:YAG laser-aided fiberotomy and low-level laser therapy in alleviating relapse of rotated incisors. Am J Orthod Dentofacial Orthop. 2014;146(5):565-72.	Excluded; non-eligible outcome
79	Kim SJ, Kang YG, Park JH, Kim EC, Park YG. Effects of low-intensity laser therapy on periodontal tissue remodeling during relapse and retention of orthodontically moved teeth. Lasers Med Sci. 2013;28(1):325-33.	Excluded; non-eligible outcome
80	Kim WT, Bayome M, Park JB, Park JH, Baek SH, Kook YA. Effect of frequent laser irradiation on orthodontic pain. A single-blind randomized clinical trial. Angle Orthod. 2013;83(4):611-6.	Excluded; non-eligible outcome

81	Lim HM, Lew KK, Tay DK. A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. Am J Orthod Dentofacial Orthop. 1995;108(6):614-22.	Excluded; non-eligible outcome
82	Marini I, Bartolucci ML, Bortolotti F, Innocenti G, Gatto MR, Alessandri Bonetti G. The effect of diode superpulsed low-level laser therapy on experimental orthodontic pain caused by elastomeric separators: a randomized controlled clinical trial. Lasers Med Sci. 2015;30(1):35-41.	Excluded; non-eligible outcome
83	Marini I, Gatto MR, Bonetti GA. Effects of superpulsed low-level laser therapy on temporomandibular joint pain. Clin J Pain. 2010;26(7):611-6.	Excluded; non-eligible outcome
84	Meng M, Yang M, Lv C, Yang Q, Yang Z, Chen S. Effect of Low-Level Laser Therapy on Relapse of Rotated Teeth: A Systematic Review of Human and Animal Study. Photomed Laser Surg. 2017;35(1):3-11.	Excluded; non-eligible outcome
85	Nobrega C, da Silva EM, de Macedo CR. Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: a placebo-controlled randomized double-blind clinical trial. Photomed Laser Surg. 2013;31(1):10-6.	Excluded; non-eligible outcome
86	Qamruddin I, Alam MK, Fida M, Khan AG. Effect of a single dose of low-level laser therapy on spontaneous and chewing pain caused by elastomeric separators. Am J Orthod Dentofacial Orthop. 2016;149(1):62-6.	Excluded; non-eligible outcome
87	Ren C, McGrath C, Yang Y. The effectiveness of low-level diode laser therapy on orthodontic pain management: a systematic review and meta-analysis. Lasers Med Sci. 2015;30(7):1881-93.	Excluded; non-eligible outcome
88	Li FJ, Zhang JY, Zeng XT, Guo Y. Low-level laser therapy for orthodontic pain: a systematic review. Lasers Med Sci. 2015;30(6):1789-803.	Excluded; non-eligible outcome
89	Shi Q, Yang S, Jia F, Xu J. Does low level laser therapy relieve the pain caused by the placement of the orthodontic separators?--A meta-analysis. Head Face Med. 2015;11:28.	Excluded; non-eligible outcome
90	Stein S, Korbmacher-Steiner H, Popovic N, Braun A. Pain reduced by low-level laser therapy during use of orthodontic separators in early mixed dentition. J Orofac Orthop. 2015;76(5):431-9.	Excluded; non-eligible outcome
91	Tortamano A, Lenzi DC, Haddad AC, Bottino MC, Dominguez GC, Vigorito JW. Low-level laser therapy for pain caused by placement of the first orthodontic archwire: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2009;136(5):662-7.	Excluded; non-eligible outcome
92	Turhani D, Scheriau M, Kapral D, Benesch T, Jonke E, Bantleon HP. Pain relief by single low-level laser irradiation in orthodontic patients undergoing fixed appliance therapy. Am J Orthod Dentofacial Orthop. 2006;130(3):371-7.	Excluded; non-eligible outcome
93	Fleming PS, Strydom H, Katsaros C, MacDonald L, Curatolo M, Fudalej P, et al. Non-pharmacological interventions for alleviating pain during orthodontic treatment. Cochrane Database Syst Rev. 2016;12:CD010263.	Systematic review; checked for eligible trials
94	Ge MK, He WL, Chen J, Wen C, Yin X, Hu ZA, et al. Efficacy of low-level laser therapy for accelerating tooth movement during orthodontic treatment: a systematic review and meta-analysis. Lasers Med Sci. 2015;30(5):1609-18.	Systematic review; checked for eligible trials
95	Gkantidis N, Mistakidis I, Kouskoura T, Pandis N. Effectiveness of non-conventional methods for accelerated orthodontic tooth movement: a systematic review and meta-analysis. J Dent. 2014;42(10):1300-19.	Systematic review; checked for eligible trials
96	Long H, Zhou Y, Xue J, Liao L, Ye N, Jian F, et al. The effectiveness of low-level laser therapy in accelerating orthodontic tooth movement: a meta-analysis. Lasers Med Sci. 2015;30(3):1161-70.	Systematic review; checked for eligible trials
97	Carvalho-Lobato P, Garcia VJ, Kasem K, Ustrell-Torrent JM, Tallon-Walton V, Manzanares-Cespedes MC. Tooth movement in orthodontic treatment with low-level laser therapy: a systematic review of human and animal studies. Photomed Laser Surg. 2014;32(5):302-9.	Systematic review; checked for eligible trials
98	de Almeida VL, de Andrade Gois VL, Andrade RN, Cesar CP, de Albuquerque-Junior RL, de Mello Rode S, et al. Efficiency of low-level laser therapy within induced dental movement: A systematic review and meta-analysis. J Photochem Photobiol B. 2016;158:258-66.	Systematic review; checked for eligible trials
99	Kalemaj Z, Debernard IC, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: a systematic review. Eur J Oral Implantol. 2015;8(1):9-24.	Systematic review; checked for eligible trials
100	Long H, Pyakurel U, Wang Y, Liao L, Zhou Y, Lai W. Interventions for accelerating orthodontic tooth movement: a systematic review. Angle Orthod. 2013;83(1):164-71.	Systematic review; checked for eligible trials
101	Sonesson M, De Geer E, Subraian J, Petren S. Efficacy of low-level laser therapy in accelerating tooth movement, preventing relapse and managing acute pain during orthodontic treatment in humans: a systematic review. BMC Oral Health. 2016;17(1):11.	Systematic review; checked for eligible trials
102	Sousa MV, Pinzan A, Consolaro A, Henriques JF, de Freitas MR. Systematic literature review: influence of low-level laser on orthodontic movement and pain control in humans. Photomed Laser Surg. 2014;32(11):592-9.	Systematic review; checked for eligible trials
103	Yi J, Xiao J, Li H, Li Y, Li X, Zhao Z. Effectiveness of adjunctive interventions for accelerating orthodontic tooth movement: a systematic review of systematic reviews. J Oral Rehabil. 2017;44(8):636-54.	Systematic review; checked for eligible trials
104	AlSayed Hasan MMA, Sultan K, Hamadah O. Low-level laser therapy effectiveness in accelerating orthodontic tooth movement: A randomized controlled clinical trial. Angle Orthod. 2017;87(4):499-504.	Included for potential evaluation
105	Caccianiga G, Paiusco A, Perillo L, Nucera R, Pinsino A, Maddalone M, et al. Does Low-Level Laser Therapy Enhance the Efficiency of Orthodontic Dental Alignment? Results from a Randomized Pilot Study. Photomed Laser Surg. 2017;35(8):421-6.	Included for potential evaluation

106	Nahas AZ, Samara SA, Rastegar-Lari TA. Decrowding of lower anterior segment with and without photobiomodulation: a single center, randomized clinical trial. Lasers Med Sci. 2017;32(1):129-35.	Included for potential evaluation

Supplementary Table 4. Communcations with trialists to request data.

Nr.	Paper	Trialist	Request	Status
1	O'Dywer L, Littlewood SJ, Rahman S, Spencer RJ, Barber SK, Russell JS. A multi-center randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 1: Treatment efficiency. Angle Orthod 2016;86(1):142-8.	Sophy Barber	Missing SDs	Provided data
2	Miles P, Fisher E. Assessment of the changes in arch perimeter and irregularity in the mandibular arch during initial alignment with the AcceleDent Aura appliance vs no appliance in adolescents: A single-blind randomized clinical trial. Am J Orthod Dentofacial Orthop 2016;150(6):928-936.	Peter Miles	Missing SDs	Provided data
3	Shedam, M. The Effect of Chewing Gum on the Pain Associated With Initial Placement of Fixed Orthodontic Appliances. J Dent & Oral Care 2015;1(1):1-5.	Mueez Shedam	Missing SDs	Provided data
4	Xu Y, Xie J. Comparison of the effects of mini-implant and traditional anchorage on patients with maxillary dentoalveolar protrusion. Angle Orthod 2017;87(2):320-327.	Yanhua Xu	Trials included in systematic review	Provided included trials

SD, standard deviation.

Supplementary Table 5. Charecteristics of included trials.

Nr	Trial	Published papers	sample	Registered	RoB_{low} for randomisation generation	RoB_{low} for blind outcome assessment*
1	AlSayed 2016	1	26	Yes	No	No
2	Al-Sibaie 2014	1	56	No	Yes	Yes (for cephalometrics)
3	Atik 2014	1	33	No	No	No
4	Benson 2007; Sandler 2008	2	47	Yes	Yes	Yes (for cephalometrics) No (for duration)
5	Benson 2012	1	57	No	Yes	Yes (probably)
6	Bhardwaj 2017	1	14	No	No	No
7	Bhatia 2014	1	24	No	No	No
8	Caccianiga 2017	1	36	No	Yes	No
9	Chen 2013	1	40	No	No	No
10	Farzanegan 2012	1	20	No	Yes	Yes
11	Feldmann 2008;2012	2	113	No	Yes	No
12	Fleming 2009a;b;c; 2010	4	60	Yes	Yes	No
13	Gokce 2012	1	18	No	No	No
14	Huang 2007	1	20	No	Yes	No
15	Ireland 2016	1	1000	Yes	Yes	Yes (patient-reported pain; patient couldn't be blinded; data entry was blinded)
16	Jiang 2009	1	46	No	No	No
17	Johansson 2012	1	90	No	Yes	Yes (for ICON) No (for duration or appointments)
18	Kaklamanos 2017	1	22	No	Yes	No
19	Kalemaj 2017	1	19	No	Yes	No
20	Leite 2012	1	38	No	No	Yes
21	Liu 2009	1	34	No	Yes	No
22	Liu 2016	1	50	No	No	No
23	Ma 2016	1	30	No	No	No
24	Mandall 2010;2012;2016	3	69	Yes	Yes	Yes
25	Marie 2003	1	48	No	No	No
26	Miles 2010	1	60	No	No	No
27	Miles 2012	1	58	No	Yes	Yes (patient-reported pain; patient couldn't be blinded; data entry was blinded)
28	Miles 2016	1	40	No	Yes	Yes (patient-reported pain; patient couldn't be blinded; data entry was blinded)
29	Nadeem 2016	1	60	No	Yes	No
30	Nahas 2016	1	34	No	No	No
31	O'Dwyer 2016	1	135	No	Yes	Yes (somewhat vaguely stated)
32	Pandis 2010	1	66	No	Yes	No
33	Pandis 2011	1	50	No	Yes	No
34	Pringle 2009	1	52	Yes	Yes	No
35	Reddy 2014	1	29	No	Yes	No
36	Sandler 2014	1	71	Yes	Yes	Yes (for anchorage loss) No (for duration)
37	Scott 2008a;b; DiBiase 2011	3	60	Yes	Yes	No (for pain) No (for PAR) No (for duration or appointments) No (for resorption)
38	Sharma 2012	1	30	No	Yes	Yes
39	Shedam 2015	1	60	No	No	No
40	Songra 2014	1	98	Yes	Yes	No
41	Su 2009	1	30	No	Yes	No

42	Upadhyay 2008a	1	36	No	Yes	Yes
43	Upadhyay 2008b	1	30	No	No	No
44	Vaughn 2005	1	32	No	Yes	Yes
45	Wei 2010	1	20	No	Yes	No
46	Woodhouse 2015a;b; DiBiase 2016	3	55	Yes	Yes	No
47	Xu 2001	1	40	No	No	No
48	Yu 2011	1	32	No	Yes	No

RoB_{low}, low risk of bias
* assessment of blind outcome assessment was performed on outcome level. Whenever no outcome is specified in this list, it pertains to the single outcome that this study contributed with in the analyses.

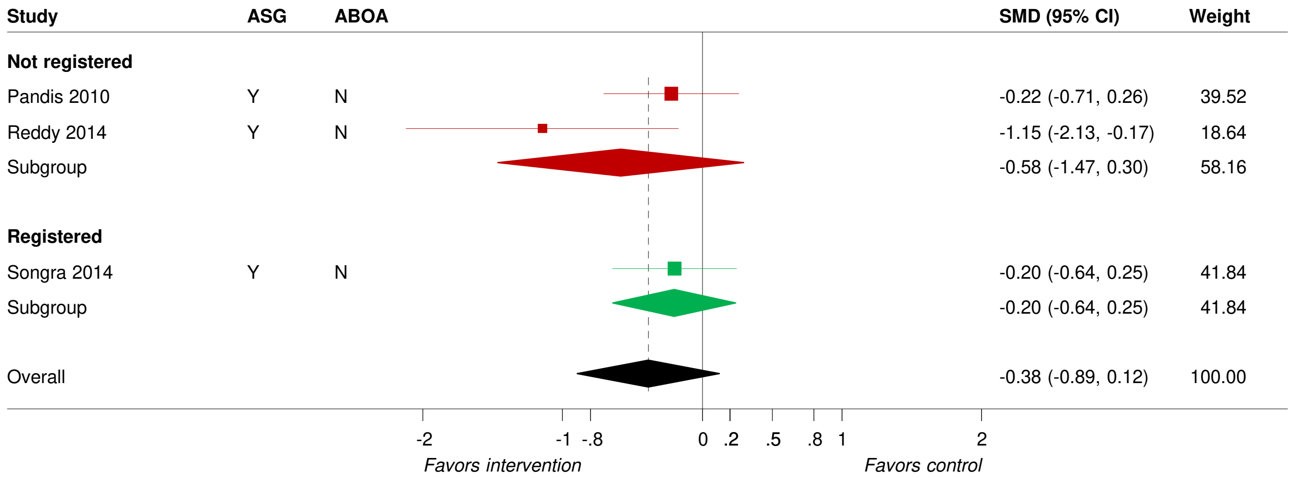
Supplementary Table 6. Details of included meta-analyses.

						Registered	
MA	**Intervention group**	**Control group**	**Condition**	**Outcome**	**Trials**	**n**	**%**
1	Active self-ligating brackets	passive self-ligating brackets	Comprehensive orthodontic treatment	Time to align the teeth	3	1	33%
2	Maxillary protraction	No treatment	Maxillary deficiency	Maxillomandibular discrepancy (ANB angle)	3	1	33%
3	Maxillary protraction	No treatment	Maxillary deficiency	Cranio-maxillary relationship (SNA angle)	3	1	33%
4	Maxillary protraction	No treatment	Maxillary deficiency	Cranio-mandibular relationship (SNB angle)	3	1	33%
5	Chewing gum	No chewing gum	Comprehensive orthodontic treatment	Pain at day 1	5	1	20%
6	Light therapy	No light therapy	Comprehensive orthodontic treatment	Time to align the teeth	3	1	33%
7	Skeletal anchorage	Conventional anchorage	Orthodontic space closure	Incisor retraction	10	1	10%
8	Skeletal anchorage	Conventional anchorage	Anchorare control	Molar anchorage loss	14	2	14%
9	Skeletal anchorage	Conventional anchorage	Anchorare control	Treatment duration	3	1	33%
10	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Pain at day 1	6	3	50%
11	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Treatment outcome with occlusal index (PAR/ICON)	3	2	66%
12	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Time to align teeth	6	3	50%
13	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Number of visits needed	6	2	33%
14	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Orthodontic induced root resorptio	3	1	33%
15	Self-ligating brackets	Conventional brackets	Comprehensive orthodontic treatment	Treatment duration	8	2	25%
16	Vibration adjunct	No adjunct	Comprehensive orthodontic treatment	Pain at day 1	4	1	25%

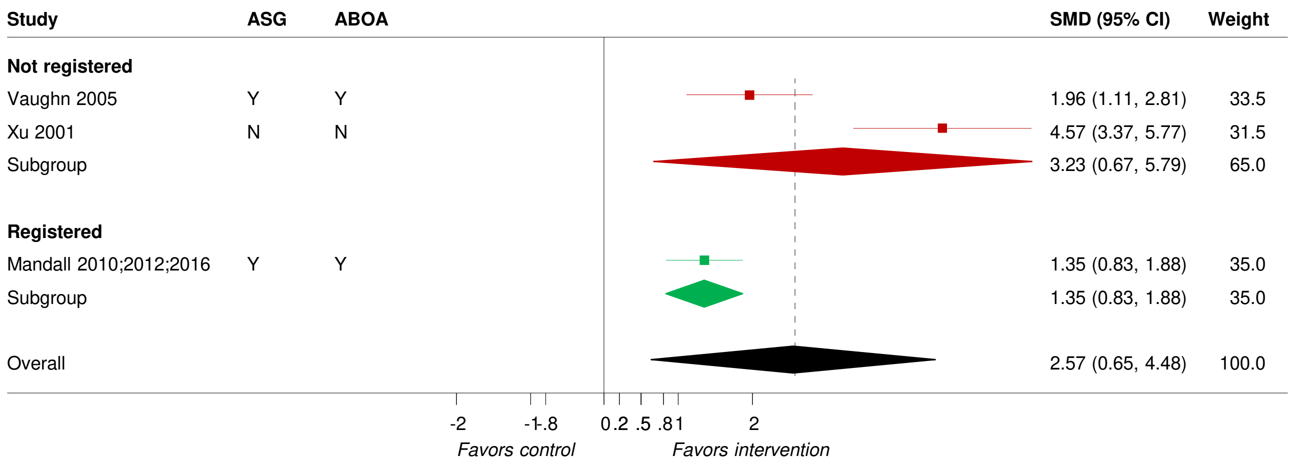
MA, meta-analysis.

Supplementary Figure. Forest plots for meta-analyses included in meta-epidemiological synthesis. ABOA, adequate blinding of outcome assessor; ASG, adequate sequence generation (randomization); CI, confidence interval; N, no; SMD, standardized mean difference; Y, yes.

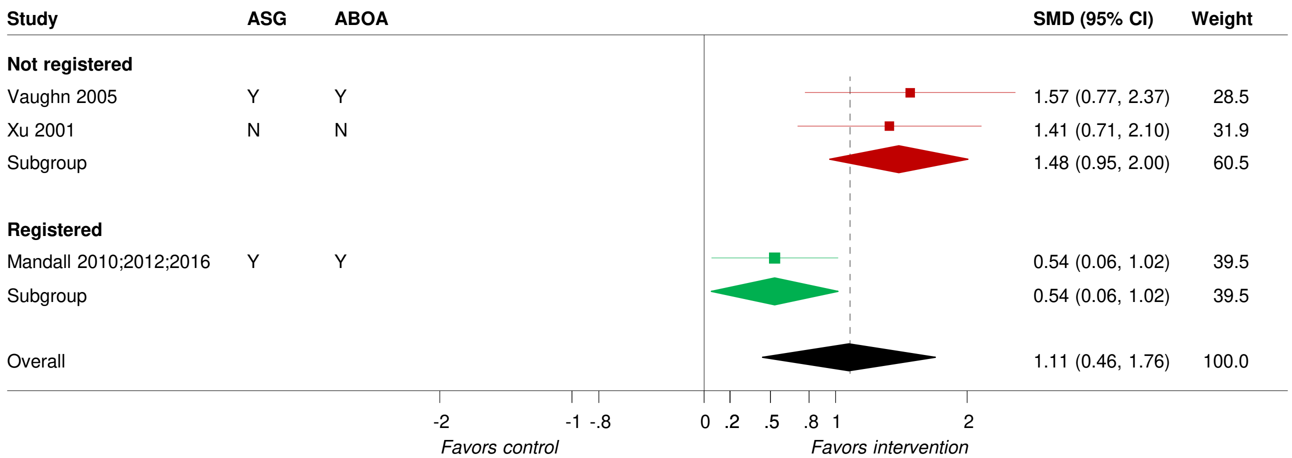
Active (intervention) versus passive (control) self-ligating brackets; outcome: time to align the teeth



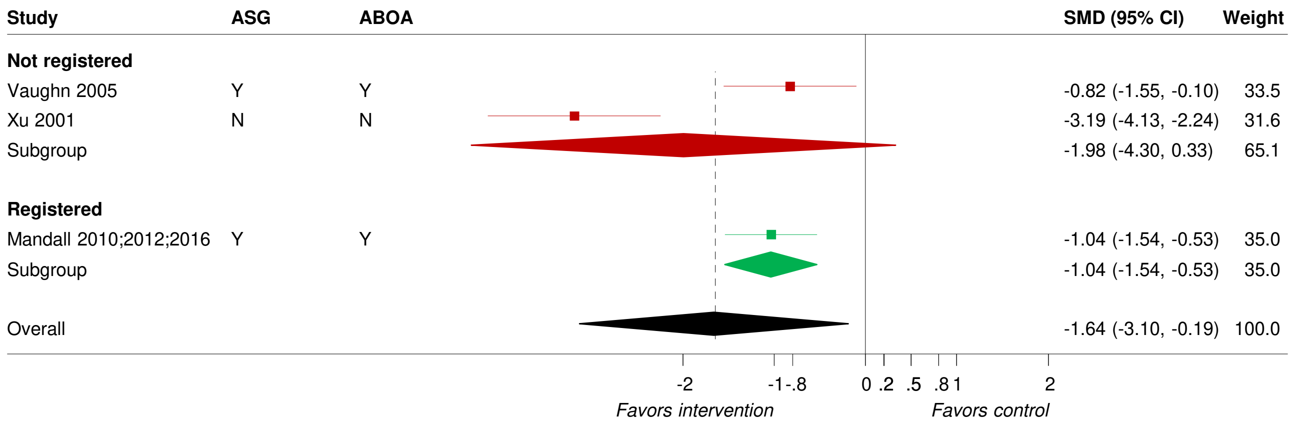
Maxillary protraction (intervention) vs no treatment (control) for maxillary deficiency; maxillomandibular discrepancy (ANB angle)



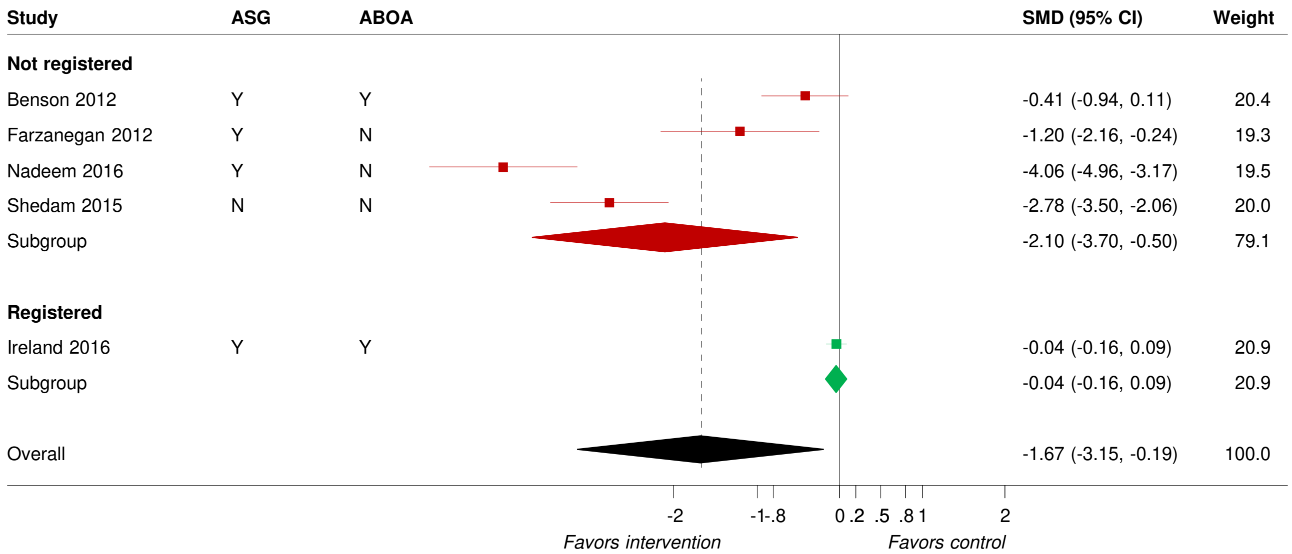
Maxillary protraction (intervention) vs no treatment (control) for maxillary deficiency; cranio-maxillary relationship (SNA angle)



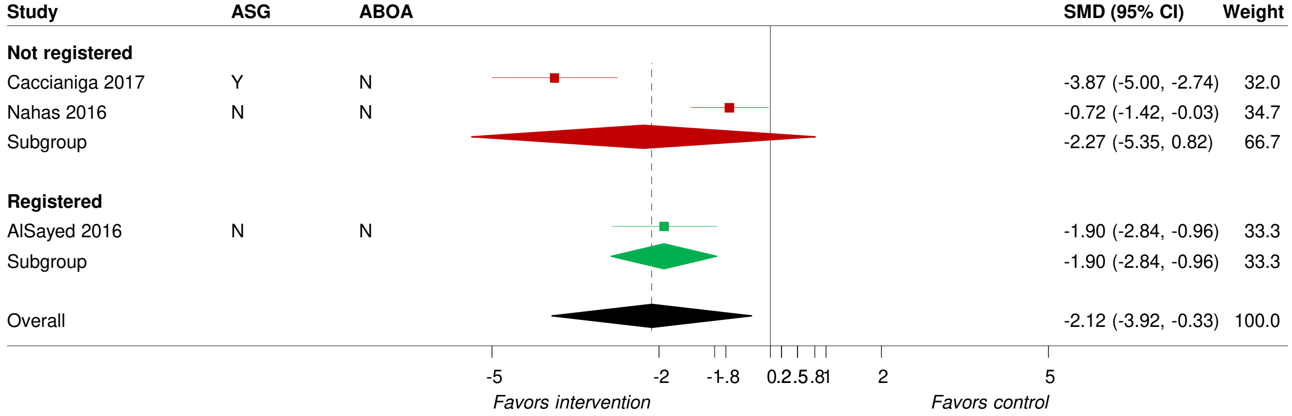
Maxillary protraction (intervention) vs no treatment (control) for maxillary deficiency; cranio-mandibular relationship (SNB angle)



Chewing gum (intervention) vs no chewing gum (control) for comprehensive treatment; pain at day 1

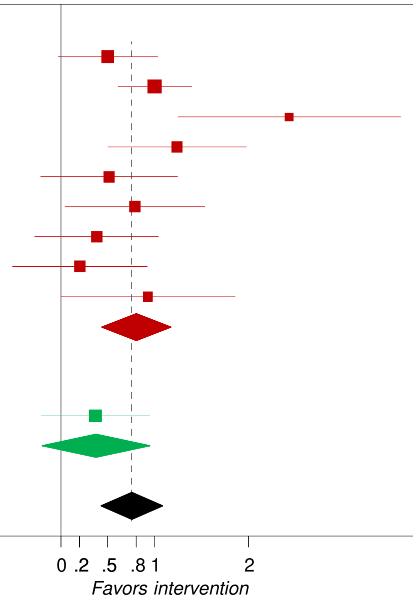


Light therapy (intervention) vs no light therapy (control) for comprehensive treatment; time to align the teeth



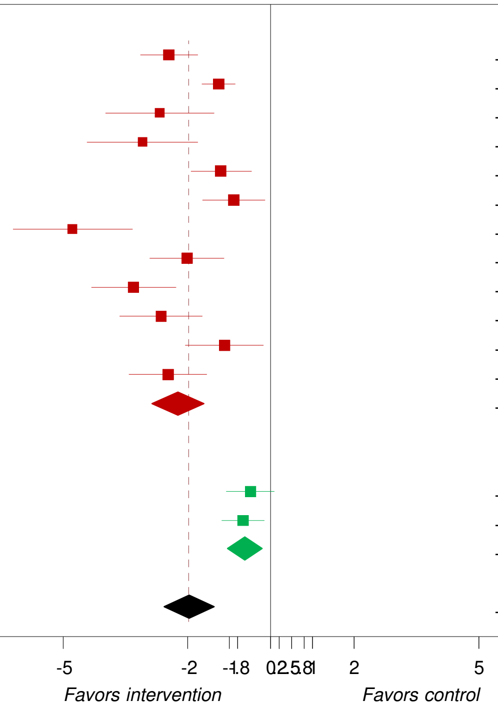
Skeletal anchorage (intervention) vs conventional anchorage (control) for space closure; incisor retraction

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Al-Sibaie 2014	Y	Y	0.50 (-0.03, 1.03)	12.2
Feldmann 2008;2012	Y	N	1.00 (0.61, 1.39)	14.2
Huang 2007	Y	N	2.43 (1.25, 3.61)	5.5
Liu 2009	Y	N	1.24 (0.50, 1.97)	9.5
Ma 2016	N	N	0.51 (-0.22, 1.24)	9.6
Su 2009	Y	N	0.79 (0.04, 1.53)	9.4
Upadhyay 2008a	Y	Y	0.38 (-0.28, 1.04)	10.5
Upadhyay 2008b	N	N	0.20 (-0.51, 0.92)	9.8
Wei 2010	Y	N	0.93 (0.00, 1.86)	7.5
Subgroup			0.81 (0.44, 1.17)	88.4
Registered				
Benson 2007; Sandler 2008	Y	Y	0.37 (-0.21, 0.95)	11.6
Subgroup			0.37 (-0.21, 0.95)	11.6
Overall			0.75 (0.42, 1.09)	100.0



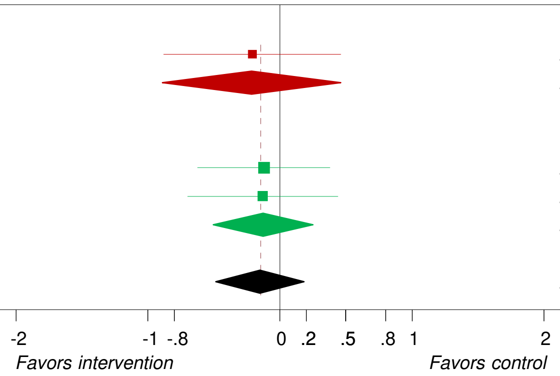
Skeletal anchorage (intervention) vs conventional anchorage (control) for space closure; molar anchorage loss

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Al-Sibaie 2014	Y	Y	-2.45 (-3.14, -1.75)	7.7
Feldmann 2008;2012	Y	N	-1.26 (-1.67, -0.86)	8.2
Gokce 2012	N	N	-2.67 (-3.98, -1.36)	6.1
Huang 2007	Y	N	-3.09 (-4.42, -1.75)	6.1
Liu 2009	Y	N	-1.19 (-1.93, -0.46)	7.6
Ma 2016	N	N	-0.90 (-1.65, -0.15)	7.5
Sharma 2012	Y	Y	-4.77 (-6.20, -3.33)	5.8
Su 2009	Y	N	-2.02 (-2.91, -1.13)	7.2
Upadhyay 2008a	Y	Y	-3.30 (-4.32, -2.28)	6.9
Upadhyay 2008b	N	N	-2.64 (-3.63, -1.64)	6.9
Wei 2010	Y	N	-1.12 (-2.06, -0.17)	7.1
Yu 2011	Y	N	-2.47 (-3.40, -1.54)	7.1
Subgroup			-2.23 (-2.84, -1.61)	84.1
Registered				
Benson 2007; Sandler 2008	Y	Y	-0.49 (-1.08, 0.09)	7.9
Sandler 2014	Y	Y	-0.67 (-1.19, -0.16)	8.0
Subgroup			-0.59 (-0.98, -0.21)	15.9
Overall			-1.98 (-2.59, -1.36)	100.0



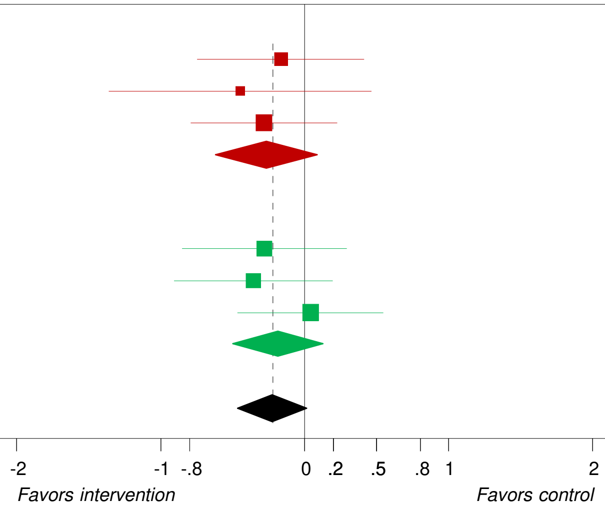
Skeletal anchorage (intervention) vs conventional anchorage (control) for space closure; treatment duration

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Liu 2009	Y	N	-0.21 (-0.88, 0.46)	23.9
Subgroup			-0.21 (-0.88, 0.46)	23.9
Registered				
Sandler 2014	Y	N	-0.12 (-0.63, 0.38)	42.9
Benson 2007; Sandler 2008	Y	N	-0.13 (-0.70, 0.44)	33.2
Subgroup			-0.13 (-0.50, 0.25)	76.1
Overall			-0.15 (-0.48, 0.18)	100.0



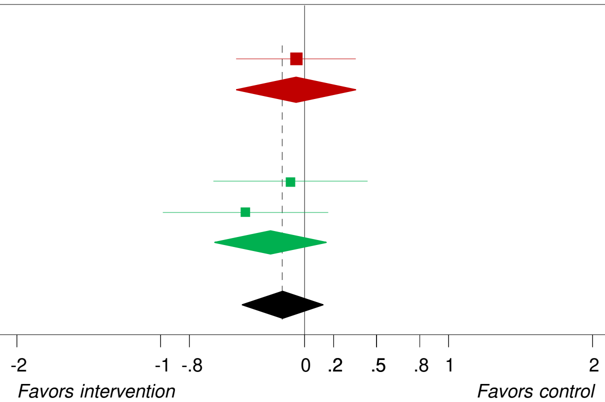
Self-ligating brackets (intervention) vs conventional brackets (control); pain at day 1

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Jiang 2009	N	N	-0.17 (-0.75, 0.41)	16.3
Kalemaj 2017	Y	N	-0.45 (-1.36, 0.46)	6.6
Miles 2010	N	N	-0.29 (-0.79, 0.22)	21.1
Subgroup			-0.27 (-0.62, 0.09)	44.0
Registered				
Fleming 2009a;b;c; 2010	Y	N	-0.28 (-0.85, 0.29)	16.8
Pringle 2009	Y	N	-0.36 (-0.91, 0.19)	18.1
Scott 2008a;b; DiBiase 2011	Y	N	0.04 (-0.47, 0.55)	21.1
Subgroup			-0.19 (-0.50, 0.13)	56.0
Overall			-0.22 (-0.45, 0.01)	100.0



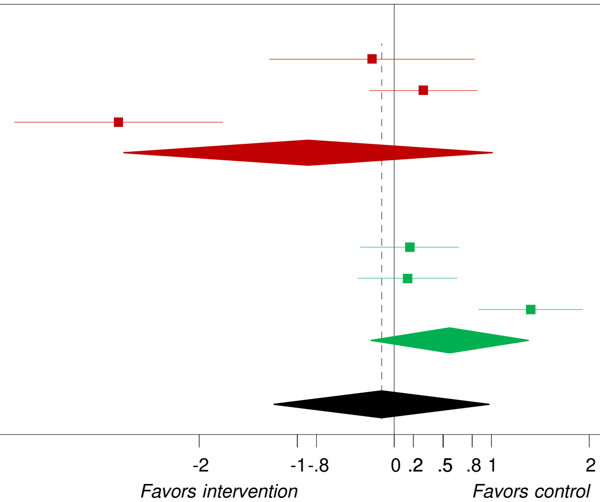
Self-ligating brackets (intervention) vs conventional brackets (control); treatment outcome with occlusal index (PAR/ICON)

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Johansson 2012	Y	Y	-0.06 (-0.47, 0.36)	47.3
Subgroup			-0.06 (-0.47, 0.36)	47.3
Registered				
Fleming 2009a;b;c; 2010	Y	N	-0.10 (-0.63, 0.44)	28.3
Scott 2008a;b; DiBiase 2011	Y	N	-0.41 (-0.99, 0.17)	24.3
Subgroup			-0.24 (-0.63, 0.15)	52.7
Overall			-0.15 (-0.44, 0.13)	100.0



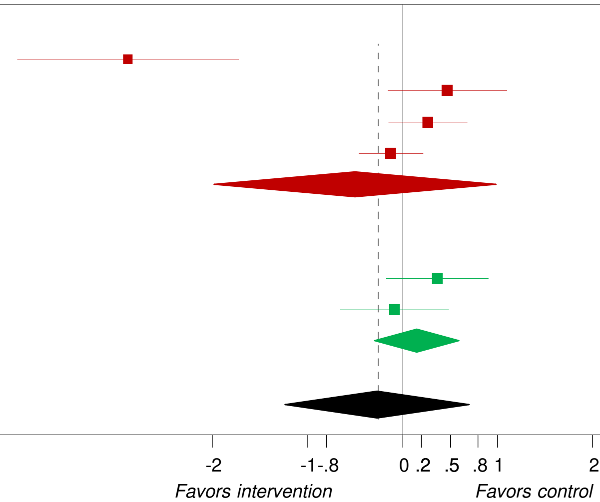
Self-ligating brackets (intervention) vs conventional brackets (control); time to align teeth

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Bhardwaj 2017	N	N	-0.23 (-1.28, 0.82)	15.5
Pandis 2011	Y	N	0.30 (-0.26, 0.86)	17.2
Reddy 2014	Y	N	-2.83 (-3.91, -1.76)	15.4
Subgroup			-0.89 (-2.78, 1.00)	48.1
Registered				
Fleming 2009a;b;c; 2010	Y	N	0.16 (-0.35, 0.67)	17.3
Scott 2008a;b; DiBiase 2011	Y	N	0.14 (-0.37, 0.64)	17.3
Songra 2014	Y	N	1.40 (0.87, 1.93)	17.3
Subgroup			0.56 (-0.25, 1.38)	52.0
Overall			-0.13 (-1.23, 0.98)	100.0



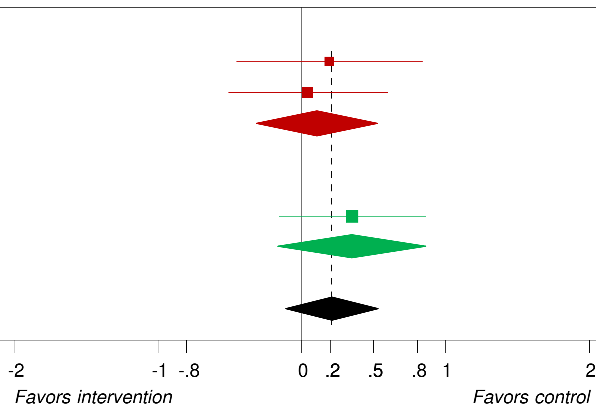
Self-ligating brackets (intervention) vs conventional brackets (control); number of visits needed

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Bhatia 2014	N	N	-2.89 (-4.06, -1.72)	14.2
Chen 2013	N	N	0.48 (-0.15, 1.10)	16.7
Johansson 2012	Y	N	0.27 (-0.14, 0.69)	17.4
O'Dwyer 2016	Y	Y	-0.12 (-0.46, 0.22)	17.6
Subgroup			-0.50 (-1.99, 0.99)	66.0
Registered				
Fleming 2009a;b;c; 2010	Y	N	0.37 (-0.17, 0.91)	17.1
Scott 2008a;b; DiBiase 2011	Y	N	-0.08 (-0.66, 0.49)	16.9
Subgroup			0.15 (-0.29, 0.60)	34.0
Overall			-0.26 (-1.22, 0.70)	100.0



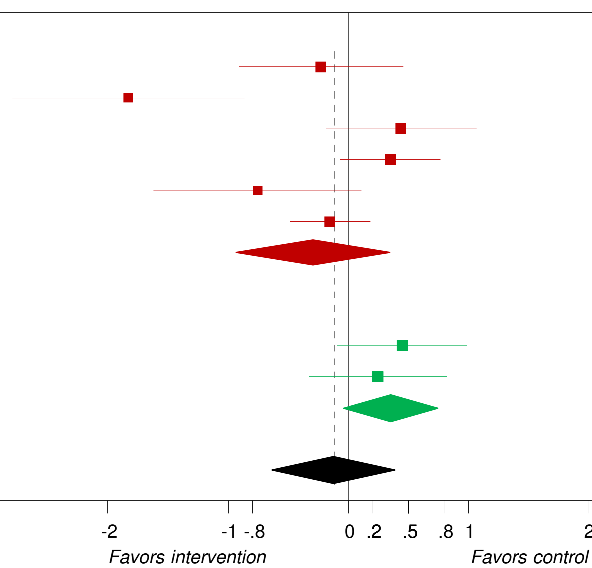
Self-ligating brackets (intervention) vs conventional brackets (control); orthodontic induced root resorption

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Leite 2012	N	Y	0.19 (-0.45, 0.84)	25.3
Liu 2016	N	N	0.04 (-0.51, 0.60)	34.3
Subgroup			0.10 (-0.32, 0.53)	59.6
Registered				
Scott 2008a;b; DiBiase 2011	Y	N	0.35 (-0.16, 0.86)	40.4
Subgroup			0.35 (-0.16, 0.86)	40.4
Overall			0.20 (-0.12, 0.53)	100.0



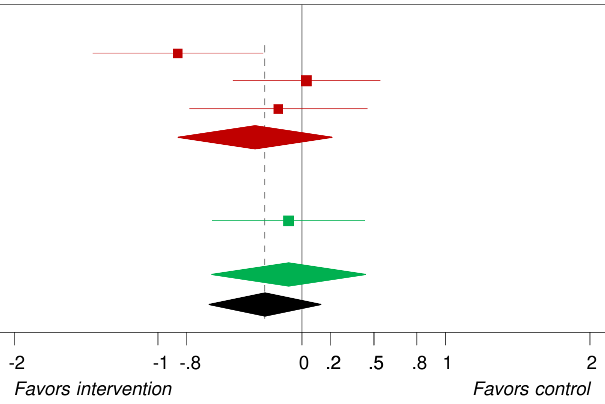
Self-ligating brackets (intervention) vs conventional brackets (control); treatment duration

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Atik 2014	N	N	-0.23 (-0.91, 0.46)	12.1
Bhatia 2014	N	N	-1.83 (-2.80, -0.87)	9.9
Chen 2013	N	N	0.44 (-0.19, 1.07)	12.5
Johansson 2012	Y	N	0.35 (-0.07, 0.77)	14.1
Kaklamanos 2017	Y	N	-0.75 (-1.62, 0.11)	10.7
O'Dwyer 2016	Y	Y	-0.15 (-0.49, 0.19)	14.5
Subgroup			-0.29 (-0.93, 0.35)	73.8
Registered				
Fleming 2009a;b;c; 2010	Y	N	0.45 (-0.09, 0.99)	13.2
Scott 2008a;b; DiBiase 2011	Y	N	0.25 (-0.33, 0.82)	13.0
Subgroup			0.35 (-0.04, 0.75)	26.2
Overall			-0.12 (-0.62, 0.39)	100.0



Vibration adjunct (intervention) vs no adjunct (control) for comprehensive treatment; pain at day 1

Study	ASG	ABOA	SMD (95% CI)	Weight
Not registered				
Marie 2003	N	N	-0.86 (-1.45, -0.27)	23.7
Miles 2012	Y	Y	0.03 (-0.48, 0.55)	27.3
Miles 2016	Y	Y	-0.16 (-0.78, 0.46)	22.5
Subgroup			-0.32 (-0.85, 0.21)	73.4
Registered				
Woodhouse 2015a;b; DiBiase 2016	Y	N	-0.09 (-0.62, 0.44)	26.6
Subgroup			-0.09 (-0.62, 0.44)	26.6
Overall			-0.26 (-0.64, 0.13)	100.0



Appendix. Author contributions and post hoc changes to the protocol.

Authors' contributions

The corresponding author had final responsibility for the decision to submit for publication. SNP and TE conceived the study. SNP, GMX, MTC, and TE extracted and sorted data for the study. SNP performed the analysis and wrote the first draft of the manuscript. All authors contributed to critical revision of the manuscript for important intellectual content and approved the final version. SNP is the guarantor.

Post hoc protocol changes

- A relative risk was calculated for the association between trial registration (original exposure variable in the protocol) and low risk of bias for the random sequence generation (original covariate to be used for covariate-adjusted analysis in the protocol). This is done to provide a measure of association between these two methodological characteristics of trials and is only shortly discussed in the Results and Discussion section.
- The additional effect of low trial risk of bias for the random sequence generation was initially planned in the protocol as a subgroup analysis. For presentation reasons, as this included the re-calculation of the effect of trial registration, while accounting for trial risk of bias, this was presented in the paper as a sensitivity analysis.
- An additional sensitivity analysis was performed by including 8/16 meta-analyses with the largest number of included trials, after finding a statistically significant Egger's test (interpreted as small-study effects). This is noted clearly as post hoc.
- The risk of bias of each trial was additionally assessed in terms of blinding of outcome assessment after comments from a reviewer during peer review. This was used to perform an additional sensitivity analysis, as was done for bias originating from the random sequence generation.